HANDBOOK OF
DIAGNOSIS & TREATMENT
OF
VENEREAL DISEASES

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BY

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PREFACE TO THIRD EDITION

THE revisions in the third edition of this handbook have resulted from the increasing knowledge of the value of penicillin therapy—and of its limitations—in the treatment of the various manifestations of syphilis and of gonorrhoea.

The introduction of oil-wax vehicles permitting a longer effective tissue concentration of the drug after a single injection, has made this form of therapy more widely applicable in out patient departments while the increasing purity of the drug has permitted greater concentration and lessened bulk, of the individual dose

On the other hand in syphilis it is now recognised that penicillin alone is insufficient, and that it must be supplemented by arseno-bismuth injections. However it seems not improbable that in the near future the isolation of the anti-syphilitic penicillin factor in a pure state may make this non toxic drug replace to an even greater extent the older forms of antisyphilitic therapy

The final evaluation of the present schemes of treatment cannot be made for a number of years and the greatest care is therefore essential to secure the adequate follow-up of all patients so treated

My thanks are again due to Dr C P Heywood for assistance in reading the proofs while to the publishers I must acknowledge my continued indebtedness for their considerateness

A E W McLACHLAN

BRISTOL
March 1947

PREFACE TO FIRST EDITION

THE present war time increase in the venereal diseases, which are statutorily defined in the Public Health (*Venereal Diseases*) *Regulations of 1916* as Syphilis Soft Sore and Gonorrhoea, renders it imperative for the individual practitioner to have an adequate knowledge of the subject In no other department of medicine is there a greater responsibility on the practitioner to maintain a constantly high index of suspicion as to the possible occurrence of a venereal disease to detect or exclude infection at the earliest possible moment by the routine application of the appropriate laboratory tests to impress upon the patient the dangers of neglect of treatment and to counsel or carry out adequate treatment and tests of cure in cases of established disease.

This volume has been evolved as the result of the systematic and clinical instructi n of undergra luate and post-graduate students over a number of years to provide a concise introduction to the principles of diagnosis and treatment of the venereal diseases suitable for the instruction of the lementary student yet adequate for the needs of the busy practitioner desirous of quickly refreshing his knowledge or treating cases in his own practice

I have to express my indebtedness to Dr J A W M Cluskie and Dr C P Heywood for their helpful criticism of the typescript and for reading the proofs and to Pr fessor R V Bradlaw for a number of the coloured illustrations. My thanks are due to the Holborn Surgical Instrument Company for the illustrations of instruments, and I gladly acknowledge the skill of Mr C Shepley in providing several coloured and black and whit drawings.

To the publishers Messrs. E & S Livingstone Ltd. an l especially to Mr Charles MacMillan I must express my great appreciation of their never failing assist nce patience courtesy and ability to overcome those difficulties peculiarly inseparable from the pres nt tim

A. F W McLACHLAN

NEWCASTLE UPON TYNE
March 1944

CONTENTS

CHAPTER I

THE COURSE OF ACQUIRED SYPHILIS

SYPHILIS is a contagious disease caused by the *Treponema pallidum* * which after penetration of the skin or mucous surface causes first a local sore then gradually invades every organ and tissue of the body with subsequent liability to early or later manifestations of the disease in any of these structures

Modes of Infection.—Syphilis may be acquired by *direct* or *mediate* contact or may be *congenital*. *Direct* infection in the majority of cases (94–95 per cent) is by sexual contact less commonly by perversions or kissing Digital contact may result in local infection or may be the means of conveying infection to other parts of the body *Mediate* infection may occur socially from imperfectly cleansed eating or drinking utensils more especially if these are cracked or chipped and liable to harbour infective material or from the common use of toilet articles professionally from glassblower's tubes assayer's blowpipes musical wind instruments, or tattooing needles. In the past infection has been conveyed by imperfectly sterilised medical, surgical, or dental instruments such cases are now unknown. Blood transfusion has been responsible for a number of infections the application of the recognised precautions should prevent such dangers in future

* Schaudinn and Hoffmann first termed the organism the *Spirochaeta pallida*. Later the term *Spironema pallidum* was adopted by Schaudinn, but as this term had already been applied to another protozoon, he invented the term *Treponema pallidum*. The terms *Spirochaeta pallida* and *Treponema pallidum* are commonly used, or the abbreviations *S pallida* or *T pallidum*

Accidental contagion is often referred to as syphilis insontium. In *congenital syphilis* infection of the fœtus occurs by transplacental passage of *T pallidum* into the fœtal blood stream

Course of Acquired Syphilis —The course of untreated acquired syphilis has for many years been divided on clinical grounds into primary secondary and tertiary stages. A better classification is into *early syphilis* comprising the primary and secondary stages together with early asymptomatic infection and *late syphilis* including all manifestations occurring more than two years after infection The stages may be summarised —

TABLE

Stage	Main Characteristics	Time of occurrence after infection	
( ) *Primary*	Local lesion at site of inoculation	o– days (Limits 9 t 90 days)	
(2) *Secondary*	Manifestations of early generalised syphilis — spirochætæmia — symptoms referable to any organ or tissue may occur Skin rashes predominate	6 weeks to (?) years	*Early Syphil* Infectivity high in general, eminently curable
Early Latent	Asymptomatic early generalised syphil		

Classification of cases of latent syphilis in the first year of infection is required for Ministry of Health Annual Reports.

Stage.	Main Characteristics.	Time f occurrence after infection.	
(3) *Tertiary*	Late manifesta tions f generalised yphilis M groups: ( ) Skin, Mucosal, Bone Muscle, Joint. ( ) Cardio-vascular Visceral. (3) Neuro-syphilis. (4) Lat l t t (asymptomatic)	(?) to 30 years (or over)	*Late Syphilis* Infectivity low Symptomatic relief, and arrest of disease often possible, with cure in variable percentage of cases.

It must be remembered that the course of syphilis does not invariably run true to type. The primary sore may be trivial and unnoticed, or may even in some cases be absent (syphilis *d'emblée*) Thus in the investigation of a patient presenting a secondary rash there may be no history or clinical evidence on searching examination of a primary sore while patients in the late stages may deny in all good faith, knowledge of any antecedent sore or subsequent skin rash In certain of these cases in males elicitation of a history of urethral discharge yielding to a short treatment may suggest the possible date of an un recognised intraurethral chancre.

CHAPTER II

THE DIAGNOSIS OF PRIMARY SYPHILIS

The Primary Sore (*Primary Chancre Chancre Hard Sore Hard Chancre Primary*)

THE common sites of infection in order of frequency are —

TABLE

Genital 94–95 per ce t of all Chancres.				Extragenital 5–6 per cent f all Chancres	
M le		Female		Sexual distribution pproximately equal	
	Per cent		Per cent		Per cent
Coronal Sulc	35 4	Cervix ter i	40–50	Lip	60–70
Inner aspect f prepuce	30–35	Labia majora	30–35	Tongue	4 5
Preputial meat	4	Labia minora	8	Tonsil	7
Shaft of peni	7	Fourchett	5–6	Finger	4 5
Frenum	5	Urethra	4	Breast and N pple	2–6
Glans penis	5	Clitoris		May occu anywhere on body from crow of head t feet	
Urinary meat	2–6	Vagina			
I tra-urethral	5	*Perigenital (fol lo ing sexual exposure)*	3		
Perigenital (re-sult f se ual xposure)	3				

Sores f th oronal sulcus frequently in 'ol dd tron both the glans penis nd the nner spect f the prepuce

Characteristics of the Primary Sore.—Following an *incubation period* of from 10 to 21 days (limits 9 to 90 days) the primary sore appears at the site of inoculation It is generally supposed that the primary stage of syphilis is unaccompanied by symptoms and constitutional dis

turbance malaise headache pains in the joints anæmia and pyrexia however occur to a greater or less degree in approximately 30 per cent. of cases more especially in women.

Commencing as a dusky red macule or infrequently as a silver spot not unlike a pinpoint area touched with pure carbolic the chancre develops in one of three ways (a) an erosion (b) an ulceration or (c) a papule which subsequently undergoes superficial erosion or deeper ulceration. Infrequently ulceration is trivial, and the appearance is that of a dry scaly papule. The characteristics of the early primary sore are (1) The sore is generally *single* Approximately 20 per cent of cases show multiple sores if multiple all the lesions show the same age characteristics. (2) The sore is *round* or *ovoid* with a greyish or dusky red granulomatous or sloughy base. Crusting may occur (3) The sore is *painless* indolent and does not bleed freely—a slight initial bleeding following cleansing is rapidly followed by an ooze of clear serum in which *T pallidum* may easily be demonstrated. (4) In 50 to 60 per cent. of cases the lesion is surrounded by a well-defined dusky pink *areola* 1 to 2 mm. broad. This areola is often made more apparent by lightly scrubbing the sore with moist gauze. (5) The blood *Wassermann reaction* at this stage is generally negative. In the absence of early diagnosis and of the institution of specific treatment, further characteristics not apparent in the early stages develop (6) *Induration* affecting first the edges of the sore and comparable to the raised rim of a coat button later involves the whole base of the sore and gradually extends beyond its limits into the surrounding tissues, giving rise to a feeling of elastic cartilaginous hardness (" Typical Hunterian Chancre ") (7) *Regional Adenitis*—a painless discrete elastic globoid swelling of the regional lymph glands occurs as a late

manifestation so also may a brawny painless indolent *lymphangitis* the colour of the overlying skin varying from normal to a dusky pink or even plum colour *T pallidum* is demonstrable in the exudate of the sore and in the gland puncture juice The *Wassermann reaction* is now almost invariably positive a serological sign of generalisation of the infection The primary sore may



Fig

Excised specimen of primary sore of prepuce showing well marked areola, ovoid shape and greyish granulomatous base

vary in size from a diameter of 1 to 2 mm up to 30 mm or more the average being possibly 7 to 10 mm Many authorities suggest that the primary sore is in general smaller and its manifestations less severe in women than in men our observations however have shown no significant sexual variation

Pathological Histology of Chancre.—The various appearances which are met with during the development of a primary sore can be correlated with the underlying pathological changes. These consist of capillary dilatation swelling and proliferation of the endothelium formation



Fig. 2.
Early primary sore of frenum. No areola, no induration



Fig. 3.
Early ulcerative primary sore of glans penis. Areola and induration absent.



Fig. 4
Areolated erosive primary sore on inner aspect of prepuce. The broad dusky-pink areola is characteristic



Fig. 5
Areolated primary sore of coronal sulcus Ulceration deeper than in Fig 4

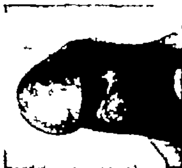


Fig 6.

Areolated primary sore with commencing induration giving rise to dome shaped appearance.



Fig 7

Primary sore showing early button-rim induration. No regional adenitis.



Fig 8

(an kimatou non ind ted sore on shaft f penis lym phang tis, nd ma ked inguinal aden



Fig 9.

Marked, painless, bra y lymphangitis may ffect the lym ph ties between the primary sore nd the reg onal gl nds.



F G o.

Primary sore of upper lip with slight induration of edge and marked lymphangitic oedema of lip nd submaxillary adenitis.



FIG 1

Healed primary sore on outer aspect f prepuce showing silver spot scar and diffuse papulo-squamous syphilide Not tendency to circular patterning of lesions

of new capillaries perivascular infiltration with small round and plasma cells and the formation of new fibrous tissue The lumen of the vessels tends to become obliterated (stage of areolation and erosion or early ulceration of *sore) The changes are at first localised and affect chiefly* the capillaries but later endarteritis and periarteritis of the larger vessels occur The cellular infiltration and fibrous tissue formation gradually extend throughout and beyond the limits of the sore Giant cell formation may *occur (Stage of induration)*

Common variations in appearance of Primary Sore.—While the majority of chancres in the male and female conform to the above description certain important variants due principally to the site of the lesion must be borne in mind In the male over 50 per cent of primary sores are subpreputial. Specific lymphangitis and œdema of the prepuce and of the dorsum of the penis may lead to an acquired phimosis and render the prepuce irretractable In the absence of gross superadded infection *T pallidum* may be demonstrated in the thin serous subpreputial discharge or by gland puncture Secondary pyogenic infection is common however and destroys the special characteristics of the sore converting it into a painful septic often ragged ulceration the subpreputial discharge becomes frankly purulent and lymphangiti and adenitis if present may show painful inflammatory changes The demonstrati n of *T pallidum* may be difficult or impos ible Severity of symptoms doubt as to the nature of th underlying lesi n or the onset of phagedena may necessi tate surgical exposure by dorsal or lateral slitting of the prepuc (p 211) If the clinical diagnosis of syphilis can be confirmed by the demonstration of *T pallidum* in the gland pur ture juic specific treatment and concomitant antiseptic sub-preputial irrigation may avert the necessity for operati n



FIG.

Crusted primary sore t site f torn frenum Induration not marked Areola bsent. Dusky red granulomatous base exposed on removal of crust



FIG. 3.

Granulomatous primary sore on outer aspect f prepuce. Sl ght localised lymphangitic oedema



FIG. 4

Early primary sore f urinary meatus (male) ith well-marked areola Induration bsent.



FIG 5

Areolated eros primary sor of female rethral orifice with early induration

Chancres of the **preputial meatus** may occur as multiple painless trivial-seeming fissures at the tip and extending towards the inner aspect areolation is absent and induration and adenitis occur as relatively late manifestations These multiple fissures may be mistaken for traumatic lesions following retraction of a phimotic prepuce.

Chancres of the **urinary meatus** may show as typical areolated circummeatal erosions. If the sore is intrameatal, the scanty serous urethral discharge and the slight pain on micturition may suggest a urethritis Careful examination will, however show a light unilateral oedema of the meatus with a raw apple appearance of the overlying mucosa of the glans In later cases unilateral induration of the meatal wall may be detected When induration is marked and the sore involves the greater part of its circumference the meatus loses its slit shape becomes circular and feels like an indurated tube

On the **shaft of the penis**, primary sores are round or ovoid. If ovoid the long axis of the sore lies transversely to the shaft of the penis. Crusting is common and suggests an impetigo or ecthyma. Removal of the crust exposes a dusky red or greyish granulomatous base Areolation is infrequent and induration occurs as a relatively late phenomenon

In the female chancres of the **cervix uteri** are most frequently single and of a superficial erosive type less commonly of the ulcerative papular and infrequently of the fungating hypertrophic or diffuse indurative types. Superficial erosive primaries are generally situated centrally around the external os they may involve either the anterior or posterior lip of the cervix alone and may extend into the cervical canal Solitary central lesions may reach a diameter of one inch or more multiple lesion may vary in size from 1 mm upwards, but seldom reach a

greater diameter than one-half inch. The colour of the erosion is dusky purplish red as contrasted with the fiery red of an acute pyogenic erosion, or the pallid red rather oedematous appearance of a chronic erosion The margin is well defined and is often encircled by a duskier red areola. The base may be covered by an adherent false membrane, removal of which is followed initially by free bleeding More commonly there is a scanty sometimes sanious mucopurulent discharge. Ulcerative papular lesions which may be single or multiple generally affect the posterior lip but may occur anywhere on the vaginal portion of the cervix. They present the same charac teristics here as elsewhere Hypertrophic types of papular chancres are rare The fungation which occurs, and the extent of the lesion suggest malignant disease. Infre quently in women known to have been exposed to infec tion, *T pallidum* has been demonstrated in the secretion of an apparently normal cervical canal—the probable explanation being a chancre in the cervical canal. The existence of an intra-cervical primary sore explains also the occurrence of a symptomless, indiarubber-like diffuse indurative oedema affecting the entire cervix *T pallidum* being demonstrable in the cervical secretion and the condition resolving under treatment.

It must be remembered that the lymph drainage from the cervix is to the common iliac and mesorectal groups of glands and that associated inguinal adenitis never occurs unless the upper portion of the vagina is involved

On the labia majora and minora, and in the region of the fourchette, typical chancrous erosions ulcerations or ulcerated papules are the rule. In a number of cases however especially on the labia the sores may be trivial in size or may occur as small atypical fissures. The prominent brawny indolent unilateral oedema which occurs early and involves the entire labium affected should



F 6
Pi mary sore in angl between ght labium majus nd minu Ea ly button rim nd ration *T pall d m* + W R negati



Fig 7
Small primary sore in ngle f litoris and labium mi us, show ng d tribution of lympha g tic oedema



Fig 8
Marked labial oedema associated with primary sores Sw lling is painless f d sky red t pl m colour nd is f braw y con stency \ papulo-squamou secondary sh prese t



F 9
Inner aspect f labium majus f same case showing tw markedly indurated primary sores
T pall d m +
W R +

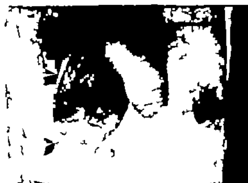


Fig. 20

Primary sores of scrotal raphe and anterior surface of left thigh *T. pallida* demonstrated in both sores despite secondary infection of chancre on thigh as shown by surrounding area of inflammation



Fig.

Primary sore at peno-scrotal junction, showing marked but ton-rim induration



Fig. 2.

Crusted, impetiginous, slightly indurated suprapubic primary sore

direct attention to the possibility of chancre Inguinal adenitis occurs as a relatively late association.

The majority of **peri-genital chancres** present no abnormal characteristics. In the perineal and peri-anal areas however painless non bleeding fissured primaries may occur with late induration and enlargement of the associated lymph glands.

Differential diagnosis of Chancre.—In the genital area there are many causes of ulceration other than primary syphilis, and many non ulcerative lesions can occur which may be confused with chancre. A primary sore must be differentiated from the later (secondary or tertiary) manifestations of syphilis from chancroid non specific ulceration following trauma pyogenic or other infection balano-posthitis (p 351) herpes progenitalis, from skin diseases *e g* scabies impetigo psoriasis from malignant disease and from certain lesions more commonly met with in the tropics The main points in the differential diagnosis are tabulated (See Insert—Table 3.)

Scabies and *impetigo* may affect the genitalia the lesions being invariably multiple In scabies scratching frequently gives rise to ulcerations, which subsequently show impetigenous crusting or an ecthymatous appearance The inguinal glands show slight tender enlargement Itching with its characteristic nocturnal periodicity and the occurrence (or history of treatment) of typical lesions elsewhere on the body complete the differentiation Impetigo can be distinguished from the impetigenous secondary changes in other genital lesions by the superficial often loosely adherent crust and the reddening without other change of the underlying tissue

Extragenital Chancres.—Chancres of the **lip** affect more commonly the lower lip The sore varying in diameter from ½ to 1 inch generally occurs in or

close to the mid-line but may appear on any part. Apposition and multiple sores are not uncommon. The crusted erosive type of chancre is most commonly met with. Removal of the crust exposes a base of dusky red granulation tissue. The discharge is scanty and sanious. On the moist inner aspect of the lip the primary sore frequently shows as a slightly raised papule covered with



Fig. 3
Areolated, erosive primary sore in centre of upper lip

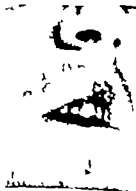


Fig. 4
Crusted erosive primary sore with marked lymphangitic oedema, causing retraction of lip

a milky or greyish white pellicle erosion or ulceration being little marked Brawny painless, rubbery lymphangitic oedema causing retraction and later eversion of the lip and typical regional adenitis of the submental and submaxillary lymph glands occur earlier than in genital chancres. Induration of the sore occurs relatively late and affects chiefly the margin of the sore

Chancres of the lip have to be differentiated on the principles already laid down from malignant disease, tuberculous ulceration from the oral manifestations of

certain skin diseases and from conditions such as herpes and thrush

Chancres of the **tongue** are generally single infrequently multiple and occur on the tip or on the dorsum near the tip The edges of the tongue or the under surface or frenum are occasionally the sites of a primary sore. Early lesions show as superficial excoriations erosions or ulcerations which rapidly become indurated Indurated papular primaries with little or well marked central ulceration or a fungous appearance may occur Enlargement of the submental submaxillary and suprahyoid glands occurs as an early manifestation.

The differential diagnosis is from malignant disease tuberculosis and traumatic ulceration

Tonsillar primaries affect the right tonsil more frequently than the left The first symptom noted by the patient is a sore throat with stinging pain and difficulty on swallowing The pain often radiates to the ear The affected tonsil shows uniform enlargement and a dusky red discoloration which often extends to the pillars of the fauces Superficial erosion or deep ulceration occurs later the affected area becoming covered with a greyish white membrane. Enlargement of the submaxillary deep sternomastoid and cervical lymph glands of the affected side constantly occurs within 10 to 14 days

The early symptoms and signs before ulceration and membrane formation appear suggest *acute tonsillitis* or *peritonsillar* abscess but raised temperature is generally absent later if membrane formation is not marked the associated glandular enlargement may suggest *sarcoma* Superficial erosion and membrane formation may simulate *diphtheria* or *mucous patches* Deeper ulceration with or without membrane may be confused with a *Vincent's infection tuberculous* or *gummatous ulceration*



Fig 5
Primary sore of dorsum of tongue, showing typical Hunterian induration.



Fig 26
Primary sore of nipple showing typical superficial keratin granulomatous lesion surrounding base of nipple

On the skin surface of the **finger** primary sores present no special variations chancre occurring in the nail fold simulates a painful onychia or paronychia with late tissue overgrowth and typical epitrochlear and axillary adenitis.



Fig 7

Ind ted papular primary sore f finger Central ulceration is t marked



Fi 8

Crusted primary sore on dorsum f second interphalangeal jo t f fifth finger

Bacteriological Confirmation of Diagnosis of Chancre.— It will be appreciated from the above descriptions that the earlier a primary sore is seen the less typical are its manifestations and the less likelihood is there of reaching an accurate diagnosis on clinical grounds alone. Clinical suspicion of the possibility of syphilis should therefore immediately be supplemented by the appropriate pathological investigations —

(1) Examination for *T pallidum* in the exudate of the sore or in the aspirate from the regional lymph glands

(2) The *Wassermann reaction* of the blood or other serological tests

The blood Wassermann reaction does not become positive for a period generally assumed to be 4 to 8 weeks after infection and may therefore be negative when the sore is seen Confirmation of the diagnosis before the

occurrence of a positive blood Wassermann reaction can only be made by the demonstration of the causal organism *T pallidum* This can most conveniently be done after the necessary experience has been gained by dark-ground illumination which permits observation of the morphological, refractile and motile characteristics of the living spirochæte and thus facilitates accurate differentiation. Staining (Leishmann Giemsa, or Fontana) collargol, and the Indian ink methods of demonstration are liable to inaccuracy and should not be used as a routine diagnostic procedure.

The Dark-ground Illumination Microscope.—A bacteriological microscope is modified by (1) the inclusion of a *funnel stop* or *iris* diaphragm in the oil immersion objective to reduce its numerical aperture to less than 1·0 (2) A centre stop is provided below the substage Abbé condenser so that only the peripheral rays are transmitted forming a hollow cone of light the apex of which is focused on the specimen to be examined. No direct light rays enter the microscopic objective. Refractile objects in the field are illuminated and viewed against a black background. Alternatively specially designed parabolodal or hemispherical (Fig 29) dark-ground condensers are used (3) A centreing device fitted to the dark-ground condenser permits alignment to the optical

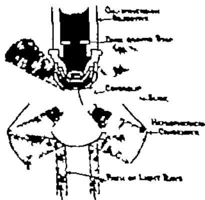


Fig. 29
Hemispherical Condenser

axes of the objective and condenser A powerful source of light is necessary e g a Pointolite electric arc or other type specially designed for the purpose.

In preparing the dark-ground microscope for the examination of a specimen the condenser must be centred. As there are various centreing devices in common use it is essential to follow exactly the instructions given by the maker of the particular type employed. It should be ascertained that the funnel stop is in position in the oil immersion objective A drop of immersion oil is applied to the surface of the condenser which is then lowered slightly The slide-coverslip preparation is placed in position on the microscope stage and the condenser is racked up so as almost to touch the slide. After application of immersion oil to the coverslip the objective is lowered and focused. The visual field may at first be indistinct and fine adjustment may be required (*a*) by widening or narrowing the pencil of light falling on the mirror and altering the angle of the mirror and (*b*) by slightly raising or lowering the condenser until the maximum illumination of objects in the field, combined with a velvety black background is obtained In microscopes incorporating an iris diaphragm instead of a fixed funnel stop this should be closed to rather more than half for the primary focusing and then slowly opened to the point of maximum brilliance. Too great an aperture is shown by a lightening of the periphery of the dark field.

Collection of Specimens for Dark-ground Examination.—Dark-ground examination may be applied to the exudate collected from an accessible open surface lesion to the fluid obtained by scarification or aspiration of a healed surface lesion or to the aspirate from enlarged regional lymph glands For satisfactory examination the specimen should be clear and contain the minimum of red blood cells or solid débris In the case of an open sore it is im

portant to obtain serum from the deeper aspects close to the areolated margin where the spirochætes are most abundant. Rubber gloves should be worn The suspected lesion is steadied between the thumb and forefinger of the left hand is thoroughly cleansed and all superficial contamination removed by mopping with pledgets of gauze moistened with saline and finally mopped dry Gentle but steady pressure is exerted at the base of the sore until a free exudate of serum is obtained If the exudate is at first obviously bloodstained this should be wiped away and the pressure maintained until an adequate clear specimen is obtained. If after cleansing pressure on the sore yields little or no serum, it is necessary gently to scarify the edge of the ulcer with a needle or a Harrison s triangular spud. In cases in which the sore is not easily accessible suction may be made after cleansing, and if necessary scarification by means of a Bier s vacuum bulb attached to a glass aspirator of suitable diameter If the exudate is free the specimen may be collected by a long capillary pipette or by Harrison s curette.

In the case of healed sores aspiration after injection of saline into the selected area of the periphery yields good specimens The technique is closely similar to that of gland puncture which may be employed in cases of healed or inaccessible sores The selected gland is fixed between the forefinger and thumb of the left hand. The point of a stout hypodermic needle attached to a syringe containing 3 to 5 minims of sterile saline solution is introduced obliquely through the skin and subcutaneous tissue into the substance of the gland. The saline is injected the gland gently massaged or manipulated between the fore finger and thumb care being taken not to dislodge the needle, and after a few moments suction is made and the specimen of tissue juice mixed with saline is withdrawn into the syringe. Dark-ground examination can also be

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In the case of healed sores, aspiration after injection of saline into the selected area of the periphery yields good specimens. The technique is closely similar to that of gland puncture which may be employed in cases of healed or inaccessible sores. The selected gland is fixed between the forefinger and thumb of the left hand. The point of a stout hypodermic needle attached to a syringe containing 3 to 5 minims of sterile saline solution is introduced obliquely through the skin and subcutaneous tissue into the substance of the gland. The saline is injected, the gland gently massaged or manipulated between the fore finger and thumb, care being taken not to dislodge the needle, and after a few moments suction is made and the specimen of tissue juice mixed with saline is withdrawn into the syringe. Dark-ground examination can also be

applied to the juice expressed from excised tissue obtained *e g* during circumcision

If immediate examination is to be carried out the serum may be taken up by direct application of a slide to the sore or transferred by a platinum loop. A coverslip is lowered on to the serum care being taken to prevent the formation of air bubbles. The preparation is covered with blotting paper and the coverslip firmly and evenly pressed down to ensure a thin film If desired the coverslip may be ringed round with vaseline to prevent currents in the field It is important that extra thin slides thickness of not more than 1 mm. and No 1 cover glasses should be used for dark-ground work

If the specimen has to be sent to a laboratory for examination a capillary tube should be used One end is gently stroked over the exudating lesion until the tube is filled to an extent of about an inch The serum is now shaken down towards the centre of the tube and both ends sealed in a flame *T pallidum* may be recognised even after several days

Identification of T pallidum.—By dark-ground illumination *T pallidum* can be differentiated with certainty and ease from the other spirochætes *T gracile T refringens T balanitidis T macrodentium T microdentium* which may be encountered in specimens obtained from syphilitic or non-specific sores in the genital or buccal regions

T pallidum is a delicate regular corkscrew spiral, varying in length from 4μ to 24μ with a breadth of approximately $0\ 2\mu$ to $0\ 25\mu$. The spirals are narrow measuring about 1μ from crest to crest the depth being slightly greater The ends are pointed Under dark ground illumination the colour appears dead white motility across the microscopic field is slow despite the vigorous movements consisting of (1) a screw like rotation

about the long axis (2) alternating expansion and closure of the coils and (3) angling, *i.e.* bending on the long axis to more than a right angle without loss of spiral form (Fig 30) *T pallidum* is morphologically indistinguishable from *T pertenue* the causal organism of yaws. *T gracile* may be confused with *T pallidum* by the inexperienced observer in that it possesses a fine regular spiral form. The coils are however coarser measuring 5 as compared with the 7 or 8 of *T pallidum* to the diameter of a red blood cell. The thickness is nearly double that of *T pallidum* angling does not occur and motility across the field is rapid.

T refringens is much coarser the spirals are irregular wider and fewer This organism is highly refractile has a greyish white colour and moves rapidly across the field.

T balanitidis is a short, rather thick highly refractile and actively motile spirochæte containing only two or three coils.

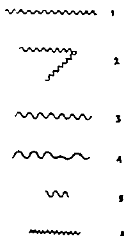


Fig 30.
Spirochæts
(1) *T pallidum.*
(2) *T pallidum* showing angling.
(3) *T gracile*
(4) *T refringens*
(5) *T balanitidis.*
(6) *T microdentium*

T macrodentium which is often found in specimens taken from the mouth is morphologically very similar to *T refringens*

T microdentium also occurs in the mouth, and may be difficult to distinguish from *T pallidum* The spirals are, however narrower and more angular the organism is more refractile and has a rusty appearance, the screw-like rotation and angling are absent

The spirilla and fusiform bacilli of Vincent's angina may be found in specimens taken from the mouth

and less frequently in genital lesions This spirochæte is rather thinner than *T refringens* the spirals are flatter and show a wide degree of distortion on movement

If *T pallidum* is not found on first examination the test should be repeated daily for 3 to 5 days during which time saline dressings or powdered sulphur are the only permissible applications If antiseptics have previously been applied to the sore hot saline foments may be used

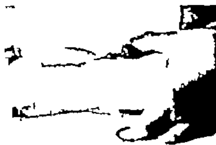
The Wassermann reaction.—As already mentioned the Wassermann reaction may remain negative for a period of from four to eight weeks after infection with *T pallidum* and therefore the diagnosis of the earliest stages of syphilis depends upon the demonstration of the causal organism. A Wassermann test should however invariably be carried out at the time of first examination The history given by the patient may be unreliable or the appearance of the sore misleading If the dark-ground examination is positive a negative Wassermann reaction is of value in prognosis and as a guide to the length of treatment required while a positive reaction confirms the diagnosis and indicates a certain degree of generalisation of the infection The application of the Wassermann reaction necessitates consideration of (1) methods of collection of specimens of blood (2) the actual test and (3) the interpretation of the result.

Collection of Blood.—In adults blood is most conveniently obtained by vein puncture. Any prominent vessel may be chosen the usual site being the antecubital fossa. The patient sits on a low stool so that the shoulder is just above the level of a table across which the arm is fully extended palm upwards. The skin should be exposed from the wrist to near the shoulder A rubber tourniquet

is applied to the upper arm is adjusted sufficiently tightly to constrict the veins, and is then fixed with an easily



Fig 3
Position of patient arm. Method of application of tourniquet and fixation of arm, distally by operator left thumb



F 3
Method of fixation of syringe when needle point is within the lumen of the vein controlling movements of patient arm and preventing flexion of elbow joint

released single loop. The patient should then clench the hand. If the veins do not become prominent they may be made to do so by instructing the patient to unclench and clench the hand slowly by gently massaging from the

wrist upwards by flicking the skin over the line of the vein or by swinging the arm vigorously. In cases in which these measures fail to make the veins stand out they may be located by careful palpation with the finger tip.

The clinician stands on the opposite side of the table facing the patient. A suitable vein having been selected, and the overlying skin sterilised with spirit or tincture of iodine, the vein is fixed by the thumb of the left hand placed an inch or so distal to the proposed site of puncture and the skin drawn taut. The fingers of the left hand are disposed round the extensor aspect of the forearm. Any attempt at flexion of the elbow which makes vein puncture difficult can be controlled (Figs. 31–32). The point of a stout hypodermic needle attached to a 5 c.c. or 10 c.c. record type syringe is pushed rapidly through the skin in the mid line of the vein and is made to travel through the subcutaneous tissue along the line of the vein for a distance of $\frac{1}{4}$ to $\frac{1}{2}$ inch, finally picking up and entering the vein. The syringe is then fixed between the thumb of the left hand and the patient's forearm and 5 c.c. of blood withdrawn. The tourniquet is released, the syringe and needle withdrawn, and the patient instructed to press firmly for a minute or two on a small pad of cotton wool placed over the site of the skin and vein punctures. This prevents hæmatoma formation or discoloration of the skin. The specimen of blood is ejected into a sterile rubber corked tube and left in a sloping position to obtain a good yield of serum.

It is important that the needle should have a short sharp sickle-shaped bevel and should be introduced through the skin bevel upwards. If the syringe and needle have been sterilised chemically, all traces of antiseptic must be removed by thorough washing with sterile distilled

water Immediately before use the syringe ... should be rinsed through with ... alternative to the syringe and needle ... blood Behring Venules—a needle attached to a ... vacuum tube—have proved satisfactory ...

If veins in the region of the antecubital ... impracticable, recourse may be made to ... back of the hand on the front of the wrist ... of the foot or on the leg. There is greater liability ... discoloration or hæmatoma formation in these ... very young children blood may be obtained from ... vein or the anterior jugular vein, constriction ... proximally being obtained by pressure from ... an assistant. Alternatively blood may be ... heel-stab. A tourniquet is applied immediately ... the knee, the skin over the pad of the heel is ... cleansed sterilised with spirit and allowed to dry ... is made into the pad of the heel with a ... sharp-pointed tenotome care being taken to ... bone. The ooze of blood is facilitated by firmly ... leg downwards from the knee A minimum ... blood should be collected

Prior to transmission to the laboratory ... name or identification number should be ... label and affixed to the specimen tube and any ... required by the laboratory entered on the ... form

The Wassermann Test.—This reaction depends ... ability of syphilitic serum to fix or inhibit the ... complement in the presence of a lipoid (antigen) ... syphilitic serum does not possess this property ... fixation or non-fixation of complement is demonstrated ... a biological indicator—a hæmolytic system. ... student is referred to a textbook of bacteriology ... details of preparation of the various reagents, and ...

technique the principles underlying the test may briefly be summarised —

(1) **System for fixation of complement** —

Patient's Serum	+ *Antigen*	+ *Complement*
(Heated for half hour at 56 C to destroy any natural complement)	(A saline dilution of cholesterinised alcoholic extract of heart)	(Fresh guinea-pig serum.)

Incubated together at 37 C

Result of incubation —

Syphilitic serum —Complement fixed by serum-antigen mixture

Non syphilitic serum —Complement remains free

(2) **Hæmolytic System**—(test for presence of free complement)

Saline suspension of well-washed sheep red blood cells	+ *Amboceptor* (Immune body) (Anti-serum obtained by repeated injection of rabbit with sheep red blood cells)

The phenomenon of hæmolysis may be summarised —

Red cells + amboceptor = no hæmolysis.
Red cells + complement = no hæmolysis.
Red cells + amboceptor + complement = hæmolysis

The addition of the hæmolytic system to the complement inhibition system indicates by hæmolysis (or non hæmolysis) after incubation at 37 C. the presence (or absence) of free complement in the latter system. Non hæmolysis is indicative of syphilitic infection and is designated as a positive reaction The test is capable of quantitative application and is generally so applied.

Interpretation of the Result of the Wassermann Reaction. —The value of any serological test in the diagnosis of

syphilis is dependent on its sensitivity and specificity While the modern Wassermann reaction has reached a remarkable degree of accuracy the sensitivity is not absolute in that a clear-cut positive reaction is not obtained in every case and in every stage of syphilis nor is the specificity absolute. Positive reactions may occur in certain diseases other than syphilis. Nevertheless, the *result of the test when considered* in conjunction with the history and clinical findings is of the utmost value as an *aid to diagnosis. The result of Wassermann investigation* is reported by the serologist as Negative (—) Positive (+) or Doubtful (±)

In undoubted syphilis a negative Wassermann reaction may occur during the first four to eight weeks of infection. Thus some 20 to 30 per cent of cases of *T pallidum* + primary sores are sero-negative on first examination. In secondary syphilis, the Wassermann reaction is almost invariably positive in late untreated syphilis, and in congenital syphilis negative serology may be found in a small percentage of cases. The Wassermann reaction becomes negative in the course of treatment of syphilis long before the disease has been eradicated. This may lead to premature discontinuance of therapy The ingestion of alcohol, and chloroform anaesthesia may temporarily convert a positive Wassermann reaction to negative this reversal does not persist for more than three days. In pregnancy and during the puerperium the blood Wassermann test may become negative or remain negative despite the presence of actively progressing syphilis.

A positive reaction is given practically only by sera from cases of syphilis. Non-specific positive reactions do however occur the commonest cause being bacterial growth in the specimen of serum Apart from this, false positive tests have been found in certain well-defined groups of conditions —

(1) *Spirochætoses* in which the infecting organism possesses antigenic properties closely similar to those of *T pallidum* and in which positive reactions are found in a high percentage of cases more especially during any febrile periods of the disease *e.g* pinta rat bite fever relapsing fever Rocky mountain fever Weil s disease and yaws In this group only Weil s disease (spirochætosis icterohæmorrhagica) and rat bite fever normally occur in this country (2) *Trypanosomiasis* (3) *Lability of the serum* an idiosyncracy peculiar to the individual which may even in normal health be sufficient to give a positive serological test or which may be predisposed to by and give positive tests in a number of intercurrent conditions, certain of which are not uncommon in this country *e.g* beri beri cancer cerebro-spinal fever cirrhosis of the liver dermatoses (psoriasis urticaria pigmentosa erythema multiforme lupus erythematosus etc) diabetes mellitus enteric fever glandular fever (infectious mononucleosis) leprosy malaria pellagra pneumonia pregnancy scarlet fever tuberculosis typhus fever and vaccination

While the incidence of false positive serological reactions has been greatly reduced by the technical improvements gradually effected in the tests and while in the absence of concomitant syphilis many of the above mentioned conditions are associated with negative serology doubtful or positive reactions may on occasion be reported leading to an erroneous diagnosis of syphilis more especially if there is for example a skin rash or other lesion vaguely suggestive of syphilis. In the majority of cases the false reaction is a transient phenomenon which rapidly undergoes spontaneous reversal but in some conditions *e g* glandular fever after vaccination or pneumonia or in serum lability a positive test may persist for two months or more The knowledge that false serum reactions may

occur in many conditions should indicate to the clinician the need for the greatest caution before accepting as incontrovertible proof of syphilis the sole evidence of an unexpected positive serological reaction. A meticulous review of the case is required:—

(1) Careful enquiry into the family and personal history and a searching clinical examination of the individual to elicit any evidence supporting a possible diagnosis of syphilis or suggesting a possible non-specific cause for the positive serological reaction.

(2) Repetition of the Wassermann reaction and other serological tests: if positive, control specimens should be examined at another laboratory.

(3) The application of special tests designed to differentiate between specific and non-specific serological reactions, e.g. the *Kahn verification test*, which relies on the principle that a specific reaction is stronger at 37° C. and weaker at 1° C., and when hypertonic saline is used in the tests instead of physiological saline the flocculation caused by syphilitic sera is increased while that of non-syphilitic sera is dispersed, or the *Harrison Richardson* modification of the Wassermann reaction, which strengthens specific but weakens non-specific reactions.

(4) In non-urgent cases, showing no clinical evidence of syphilis, the serological reactions should be consistently positive for a period of three months before reaching a diagnosis of syphilis and advising treatment. In certain cases, e.g. pregnancy, when delay might be prejudicial, treatment may be instituted at an earlier date after consultation with the obstetrician and full explanation of the position to the patient.

A doubtful reaction, often designated as weak positive, is neither negative nor positive. No diagnostic significance can therefore be attached to it, but the suspicion of the clinician should be aroused and further investigation

made In addition to the review of the history and clinical findings the test should be repeated If the result is still anomalous a provocative injection of neoarsphenamine may be given to reactivate the Wassermann reaction This injection should not be given unless the duration of the condition is sufficiently long to expect normally a positive test in cases of syphilis. An average dose of neoarsphenamine is injected intravenously and the blood test is repeated 5 to 7 days later This procedure frequently provokes a positive Wassermann reaction in cases of early or latent syphilis.

Anti-complementary reactions may sometimes be reported by the serologist The result of the test cannot be read in these cases because the serum has acquired anti complementary properties *i e* the ability in itself to fix complement The main reasons for this are hæmolysis of the blood specimen from bacterial contamination from admixture of water *e g* syringe not washed out with saline immediately prior to taking specimen or from undue shaking of the tube during transit to the laboratory Traces of chemicals (especially arsenicals) in the syringe conditions such as jaundice or uræmia and withdrawal of blood during the period of digestion of a meal when a highly chylous serum is obtained are other causes.

The interpretation of reports on the Wassermann reaction may be summarised —

(1) A single negative report is frequently of little value in the exclusion of a possible syphilitic infection

(2) A positive report in general indicates infection with syphilis this does not indicate that the lesion under *consideration is necessarily due to syphili (cf the not* infrequent association of lip or tongue cancer with late syphilis) or that the disease is active

An unexpected positive Wassermann report in cases of routine blood test or when the history and clinical

findings do not suggest syphilitic infection should lead to repetition of the test and review of the case

(3) The Wassermann reaction (and other serological tests) are laboratory aids to diagnosis and not a substitute for clinical investigation. Serological reports should therefore be considered in conjunction with the entire clinical picture.

(4) To complete the exclusion of syphilis in a patient who has been exposed to infection serological tests should be repeated over a period of at least three months.

Flocculation or Precipitation Tests.—For a number of years flocculation or precipitation tests have been applied to the diagnosis of syphilis The technique is less complicated than that of the Wassermann reaction consisting of a simple serum-antigen mixture. In the case of syphilitic serum, aggregation of particles occurs causing a flocculate or precipitate. The strength of the reaction is gauged by the density of the flocculate The Kahn Meinicke Sachs-Georgi, and Dreyer and Ward (Sigma Test) are the best known and are often applied to supplement the Wassermann reaction. The results of the tests run parallel in 90 to 95 per cent. of cases. In our experience in early syphilis positive reactions may occur later than in the Wassermann reaction, and persist for some time during treatment after the Wassermann reaction has been rendered negative

CHAPTER III

THE DIAGNOSIS OF EARLY GENERALISED (SECONDARY) SYPHILIS

FROM the moment that *T pallidum* penetrates the skin or mucous membrane there is a steady progress towards generalisation of the infection The organism multiplies at the site of inoculation extends at first by the lymphatics and later enters the blood stream causing a true spirochætæmia in which every organ and tissue of the body is liable to invasion Manifestations of this wide dissemination may occur within a few days of the appearance of the primary sore or may be delayed for several months. The secondary stage of syphilis is characterised by the occurrence of constitutional symptoms and skin rashes. Infrequently serious involvement of a viscus may occur

The **constitutional symptoms,** which are met with in 50 per cent of women and 25 per cent of men in general immediately precede the onset of the skin rash. Diffuse headache subject to nocturnal exacerbation anorexia nausea vomiting constipation and bone muscle or joint pains are the symptoms most frequently experienced *Fever of an intermittent or continuous* type may occur in these cases the temperature seldom rises above 100° to 101 F Secondary anæmia and menstrual irregularities are frequent in women. In the majority of cases the systemic symptoms are mild occasionally however they may be marked and of more serious import Persistent intense occipital headache associated with stiffness of the neck may indicate early basal meningeal involvement or the onset of jaundice may be symptomatic of a mild or progressive hepatitis

Transient albuminuria is not uncommon an acute nephritis may be met with occasionally These visceral affections will be dealt with later

Eruptions affecting the skin or mucous membranes are the most prominent feature of early generalised syphilis occurring in over 80 per cent of cases. While an almost infinite variety of clinical appearances may be met with secondary rashes fall into well-defined groups and present present definite characteristics. In the early stage of generalisation the *roseola* or *macule* as the individual element while the basis of later rashes is generally the *papule* The underlying pathology affords the explanation When in the process of blood-stream dissemination *T pallidum* reaches the skin vessels the same sequence of changes occurs as in the primary sore The stage of capillary dilatation with endothelial swelling and proliferation is recognisable clinically in the roseolar or macular rash. The later perivascular cellular infiltration partial or complete arterial occlusion revascularisation and fibrous tissue deposition, gradually extending throughout the individual lesions are manifested by the variations of the papular rash The rapidity and extent of progress, the duration and appearances of the secondary muco-cutaneous lesions depend on (1) the virulence of the infecting organism and the resistance of the tissues and (2) the possibility of successive waves of spirochætæmia and of varying numbers of organisms lodging in different portions of the skin. This explains why the roseola may in some cases fade within 24 to 48 hours and in other cases progress in a period varying from a few days up to several weeks through a maculo-papular stage to papule formation These factors also account for recurrent eruptions and for the simultaneous co-existence in one area of skin, of roseoles macules and papules (pleomorphism)

Classification of Secondary Eruptions.—The secondary skin rashes fall clinically and pathologically into two main groups connected by an intermediate transitional group These main groups and the principle sub-groups may be summarised —

(1) *Macular*	Roseolar *Recurrent Roseolar* Pigmentary	The macule is the *predominating element* in 50 per cent of secondary syphilitic rashes
(2) *Maculo-Papular*		Maculo-Papules predominate in 25 per cent
(3) *Papular*	Smooth Squamous. Vesicular or pustular Ulcerative Hypertrophic.	Papules predominate in 25 per cent

Characteristics of the Early Skin Eruptions.—The cutaneous manifestations of early generalised syphilis invariably present certain features which greatly assist in their differentiation from the diseases which may be closely imitated These characteristics are —

(1) *Distribution* —A bilaterally symmetrical distribution occurs affecting typically the flexor surfaces of the body In the early stages diffuse generalisation may give rise to wide areas of erythema later a tendency to localisation is seen Macular rashes are commonly limited to the flanks abdomen shoulders arms and chin Papular rashes frequently involve in addition the face palms and soles.

(2) *Size and Configuration* —The individual lesions are circular in outline and vary in diameter from 3 to 20 mm They may be discrete or confluent When the distribution is widespread no characteristic arrangement can be seen

the more discrete rashes show a marked tendency to be patterned in circles or in segments of circles.

(3) *Colour* —Macular lesions are of a cold pink or dusky rose colour most marked at the centre and fading into the normal skin colour at the periphery The papular rash shows the same tint in its early stages but as the lesions progress a characteristic dull red coppery or raw ham appearance develops. Subsequent pigmentary changes may cause a further alteration to a brownish-red coloration of the lesions.

(4) *Induration* —Papular lesions alone show induration which is best detected by passing the finger tip lightly from normal skin over the lesion The induration is found to be limited to the extent of the papule and involves the entire thickness of the underlying skin

(5) *Symptoms* —On the skin, secondary eruptions are painless and cause no symptoms. Tenderness may be complained of in mouth lesions while severe itching or burning is not infrequently associated with moist papules or condylomata at the ano-genital muco-cutaneous junctions.

(6) *Pleomorphism* —With the exception of the earliest skin rash which may be composed purely of roseola polymorphism—the occurrence at the same time and in the same sector of skin of roseoles macules and papules—is usual and is characteristic of syphilis alone.

(7) *Adenitis* —Glandular enlargement occurs in association with early generalised syphilis and in 80 per cent. of cases one or more of the subcutaneous groups of glands shows palpable enlargement. Involvement is bilaterally symmetrical of less degree than the adenitis associated with the chancre but presenting the same painless globoid india rubber like characteristics. The posterior cervical sub-occipital, and the epitrochlear groups are most constantly affected. Suppuration never

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occurs except as the result of superadded pyogenic infection

(8) *Pathological Confirmation* —*T pallidum* is easily found in dark-ground preparations made from secondary papular eruptions in the roseolar and macular rashes however the spirochæte may be difficult to demonstrate The blood *Wassermann reaction* is invariably positive.

(9) *Therapeutic Test* —Specific treatment causes rapid involution of the cutaneous manifestations of secondary syphilis It must be remembered that certain other skin diseases may react similarly and that the therapeutic test alone is therefore insufficient to substantiate a diagnosis of syphilis.

Differential Diagnosis of Secondary Eruptions.—All known forms of skin disease may be imitated by syphilis so much so that it is a common practice to describe the syphilitic manifestations by the name of the condition simulated *e g* morbilliform syphilide psoriasiform syphilide etc It is of the greatest importance to be able to detect the syphilitic counterfeit In this the pleomorphic nature of the skin lesions of syphilis preventing completely accurate reproduction of and the absence of symptoms and signs characteristically associated with the disease simulated should indicate the possibility of syphilis.

Roseolar Syphilides must be differentiated from —

(1) *The Eruptive Fevers* (*Scarlet Fever Measles German Measles*) —The vivid scarlet punctate erythema of *Scarlet Fever* occurs in association with a temperature of 103 to 104 F headache vomiting and characteristic strawberry tongue The rash commences on the neck and upper part of the chest and rapidly becomes more diffuse and brilliantly coloured than the syphilide. In *Measles* the lesions are at first small red spots which rapidly coalesce forming irregular crescentic blotchy patches. Temperature coryza conjunctivitis and Kop-

like spots on the buccal mucosa constantly occur In *German Measles* the frequent absence of temperature and the association of marked posterior cervical and occipital



FIG 33.
Diffuse morbilliform roseolar syphilide The centre of each macule is markedly erythematous and fades imperceptibly peripherally into normal skin

adenitis with a rose-coloured morbilliform or scarlatiniform eruption may at first suggest syphilis. The rash is transient fading in from one to three days and leaving slight staining The epidemic occurrence of rubella the slight

tenderness and more rapid enlargement of the glands the absence of other physical or serological evidence of syphilis should suggest the true diagnosis

(2) *Erythema Multiforme* —The lesions are brighter in colour and characteristically affect the backs of the hands and forearms the face and the feet Central vesiculation is frequent In the mouth bullous lesions occur which after rupture leave moist areas suggestive of the mucous patches of syphilis The onset is sudden and there may be a history of recurrent attacks There is no itching but the individual lesions may be somewhat tender

(3) *Urticaria and Drug Rashes* —The transient character of the wheals and the intense itching serve to differentiate *urticaria* Drug rashes *e g* following *sulphonamide* administration are of short duration and clear up rapidly on discontinuing the drug The eruption is more diffuse and more brilliant in colour than the roseolar syphilide. Itching is usual. Thi possibility must be borne in mind in cases of gonorrhœa under treatment

(4) *Pityriasis Rosea* —The individual lesions may vary markedly in size and are oval with the long axis parallel to the direction of the ribs The colour is at first reddish pink but a the centre of the lesion involutes it shows a yellowish tinge with a rose pink border Fine scaling is invariably present The history may be obtained of a herald patch preceding the generalised eruption by ten to fourteen days

Pigmentary Macular Syphilide. (*Leucoderma Syphiliticum*)—Thi may be due to (1) deposition of pigment in the macules without change in the intervening skin (2) diffuse hyperpigmentation with vitiligo or (3) destruction of pigment in the macules simulating vitiligo Oval areas of whitish skin varying in diameter from one quarter to three-quarters of an inch surrounded by areas of hyperpigmentation produc a mottled appear

ance. These pigmentary changes affect the region of the neck and anterior axillary fold occur almost invariably in women and are pathognomonic of syphilis. Leucoderma tends to persist indefinitely despite treatment.



FIG. 34
Pigmentary macular syphilide, showing hyperpigmentation localised to area of lesions

Maculo-papular Syphilides represent a transition stage between the macule and the papule commencing papule *formation being de*tected in the centre of the macule. They affect chiefly the trunk and limbs the face, the palms and soles being rarely involved. In general, they simulate urticaria and drug rashes from which they must be distinguished.

Papular Syphilides may occur as a further stage in development of the macular syphilide or may arise independently The individual lesions may be small (under three-eighths of an inch in diameter) in which case the distribution is diffuse or large (over one half inch in diameter) the distribution being more discrete and the lesions *tending to occur in circles or in segments of circles.* The papule is indurated and almost invariably shows a dull red copper or raw ham colour At first the lesion is smooth and non-scaly but as the underlying vascular changes progress scaling occurs later pustulation may result from liquefaction of the centre of the papule, or central ulceration and crusting lead to the impetigenous ecthymatous or rupial syphilide. In certain cases the centre of the papule may heal, giving rise to an annular



FIG. 55

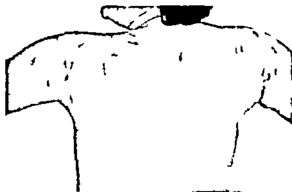


FIG. 56
Maculo-papular secondary rashes



F 37

Maculo-papular syphilide. Papule formation is seen in the centre of the macules A tendency to circinate arrangement of the eruption is noted



Fig 38

Smooth, non-scaly papular syphilide simulating papular eczema The papules show commencing central ulceration



Fig 39

Smooth non-scaly papular syphilide simulating lichen planus

appearance. Hypertrophic forms occur rarely and consist of fungoid or cauliflower like upgrowths from the infiltrated skin (Frambœsiform syphilide.)

The **common variants** of the **papular syphilides** and the **diseases simulated** may be summarised

Type of Papular Syphilide	Diseases simulated and Clinical Differentiations
(1) *Smooth Papular Syphilide* (Non Scaly)	*Lichen Planus*.—Angular flat topped, often umbilicated papules occur The colour is violaceous Itching may be intense There is no induration or pleomorphism of the lesions. *Papular Eczema* —The papules are red non indurated, itchy and pursue a chronic course Vesicular lesions may occur The distribution affects typically the extensor surfaces of the extremities *Erythema Multiforme*
All Papular Syphilides are symptomless, indolent indurated pleomorphic and of typical red copper colour Constitutional disturbance is absent or slight *T pallidum* demonstrable and the blood W assermann reaction invariably positive	*Seborrhœic Dermatitis* — Irritable, yellowish somewhat greasy non-infiltrated round or oval lesions occur chiefly on chest, interscapular areas, and the flexures A ringed appearance is common The scalp invariably shows an early seborrhœa. *Psoriasis* —The red coloured lesions are covered with silvery scales and occur more frequently on the extensor aspects of the limbs—especially the elbows and knees Extensive configurate lesions may occur on the trunk The face is rarely involved Scale formation is more marked in psoriasis on careful removal of the scales multiple capillary bleeding points are encountered
(2) *Squamous Syphilide* (Scaly)	*Scabies*.—Nocturnal itching the widespread distribution and the presence of burrows in the web of the fingers and on the wrist indicate scabies Ulceration and ecthymatous lesions may occur from scratching and subsequent pyogenic infection

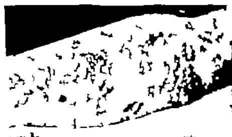


FIG 4



FIG 4



FIG. 42

Diffuse papulo-squamous eruptions simulating psoriasis Fig 40 shows close simulation of psoriasis Figs 4 and 4 show general distribution



Fig 43
Papulo-squamous secondary rash of arm and palms On the palms the lesions present the same characteristics [illegible] be [illegible] be [illegible] the body

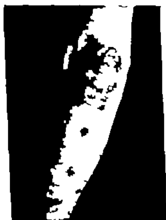


FIG 44
Pustular syphilide of back of elbow showing unruptured and recently ruptured pustules.



FIG 45
Pustular syphilide of neck. Lesions suggest molluscum contagiosum.



FIG 46
Molluscum like pustular syphilide on back of thigh (same patient as 47)



FIG. 47
Impetigenous syphilide following pustular syphilide on calf

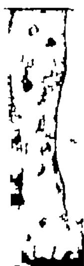


FIG 48
W id pr d imp tig syphilide (le



FIG. 49.
Impetigenous secondary syphilide localized t nose l ps, d chin

Type of Papular Syphilide.	Diseases simulated and Clinical Differentiations.
	Smallpox. — The non-indurated papular rash appears, shortly after the subsidence of the febrile prodromata, on the face and the wrists, etc. Generalisation is rapid, and the papules pass through a vesicular pustular and crusted stage. On the trunk, inflammatory areolation of the lesions may occur. In any area the lesions of smallpox are similar in size and development, as opposed to the pleomorphic variation of syphilis. The two diseases may be almost indistinguishable clinically and the differentiation may depend on the recognition of the chancre and on the laboratory tests. Isolate if in doubt.
(3) *Pustular Syphilide*	*Pustular Acne* is confined to the face back, and chest. The long duration the presence of comedones, and the pitted scars of former lesions complete the differentiation.
	Impetigo occurs on the uncovered parts of the body. Removal of the crusts show no underlying papule.
(4) *Ulcerative Syphilide* (Impetiginous) (Ecthymatous)	*Ecthyma* generally occurs in debilitated persons or at the extremes of life. The legs and buttocks are commonly affected. The lesion is initially vesicle which goes on to pustulation and rapidly becomes crusted. Removal of the adherent crust shows superficial, saucer-like ulcer with raised edges, and raw base in contrast to the deeper ulceration with edges at right angles to the skin and the unhealthy granulation tissue base of the ecthymatous syphilide.
R[illegible] Syphilid	*Bromides and Iodides* may cause inflammatory pustular acneiform lesions which may be confused with the pustular syphilide. Ingestion over long periods may lead to granulomatous, fungating lesions most commonly on the legs. These appear ances contrast sharply with the



FIG. 49.
Impetiginous secondary syphilide localised to nose, lips, and chin



Fig. 5
Ulcerative, ecthymatous secondary papular syphilide, occurring six months after infection. Note the lymphangitis of the dorsum of the penis.



Fig. 53
Hypertrophic syphilide. The lesion at the base of the nose shows organised outgrowth.

MUCOUS MEMBRANE AND MUCO-CUTANEOUS MANIFESTATIONS OF EARLY GENERALISED SYPHILIS

At any time after the early generalisation of a syphilitic infection and most commonly concurrently with the appearance of the skin eruption evidences may be found of involvement of the buccal mucous membrane or of the muco-cutaneous junctions of the lips, nose, anal orifice and vulva. These manifestations correspond to the maculo-papular or papular skin eruption, modified by a moist situation. Moist lesions are the most contagious of all syphilitic manifestations, the loss of continuity of the integument permitting the free exudation of large numbers of spirochætes. Every precaution must, therefore, be taken during their examination. The common manifestations are :—

Buccal Mucosa —(1) Diffuse Erythematous Pharyngitis (2) Mucous Patches (3) Moist Papules.

Muco-cutaneous Junctions —

Buccal Nasal —Moist Papules

Anal Vulval —(1) Moist Papules (2) Condylomata Lata.

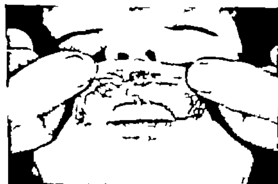
In 80 per cent of cases **a diffuse erythematous pharyngitis** occurs and is frequently associated with tonsillitis and laryngitis. A chronic sore throat with slight pain or discomfort and dysphagia is complained of The voice may be husky High temperature or rapid pulse is seldom found and the patient is less ill than would be expected from the appearance of the throat. A diffuse inflammatory redness is found on examination and there are often patches of thin greyish pellicle like exudate over the tonsils and pillars of the fauces. Enlargement of the posterior cervical and sub-occipital lymph glands is constant Mucous patches or moist papules may occur in association with diffuse erythematous pharyngitis and a careful examination of the inner aspect of the lips the palate and the dorsum of the tongue should be made.

Mucous Patches correspond to the maculo-papular or early papular skin lesions. The mucous patch is circular in outline varying in diameter from 5 to 10 mm and has a slightly raised milky or greyish flat top Induration of the base is absent Erosion of the surface occurs rapidly giving rise at first to a peripheral red rim and later to a uniform dull red patch covered by greyish-white secretion Ulceration seldom occurs, except as the result of irritation from carious teeth or from pyogenic infection. The common sites in order of frequency are the inner aspect of the lips especially at the angles the tonsils the gums the dorsum and under surface of the tongue the hard and soft palate

Moist Papules in the mouth have a similar distribution



FIG. 54.
Uneroded mucous patch on under aspect of tip of tongue.



F 55
Ulcerated mucous patches on inner aspect of pper l p and f angles of mouth

and appearance but are more elevated and have a definitely indurated base corresponding to the indurated skin papule. Central necrosis is frequent causing ulcers with a slightly raised edge and dull red base Coalescence of mucous patches or moist papules in circinate or serpiginous formation frequently occurs on the tonsils subsequent ulceration giving rise to typical *snail-track ulcers*

At the nasal and oral muco-cutaneous junctions moist



F 56
Muc us patches of inner aspect f lower lip with commencing peripheral erosion



Fig 57
Moist papules f dorsum of tongue

papules generally remain discrete but tend to become hypertrophic and often develop a wart like appearance.

Condylomata Lata represent further hypertrophic development of the moist papule In the peri anal area and on the inner aspect of the labia majora they become flat topped raised broad based lesions of a greyish white colour In patients of uncleanly habits they may extend to the perineum and scrotum in the male and to the perineum natal cleft and inner aspect of the thighs in the female Coalescence may give rise to sessile vegetative plaques

Moist papules or condylomata lata may occur on the



Fig 58
Condylomata lata of anus, inner aspect of buttocks, and scrotum



Fig 59
Vulval condylomata lata



Fig 60
Moist papules in axilla

potentially moist areas of skin *e g* in the axilla under neath the pendulous female breast and in the web of the fingers or toes While they most commonly occur in association with a papular skin rash they may persist as the only external manifestation of secondary syphilis.

DIFFERENTIAL DIAGNOSIS OF MUCOSAL AND MUCO-CUTANEOUS LESIONS OF EARLY GENERALISED SYPHILIS

The sore throat of early syphilis must be distinguished from acute tonsillitis or if there is much obvious pellicle formation from *diphtheria* or *Vincent s angina* In the absence of mucous patches or moist papules clinical differentiation may be difficult or impossible unless enquiry and inspection are made to discover the skin syphilide or the primary sore. The chronic course and mild con stitutional symptoms should suggest the possibility of syphilis more especially if swabs are negative and there is no response to the usual measures.

Mucous Patches and *moist papules* have to be differenti ated before erosion from *thrush* the mucosal lesions of certain skin diseases *e g lichen planus* and from the buccal lesions accompanying *sulphonamide* skin rashes and after erosion from *aphthous ulcers herpes* and the buccal manifestations of *erythema multiforme*

Thrush is most common in young children but may occur in adults. Raised milk like or curdy spots are seen on the tongue and inner aspects of the cheeks Coalescence may give rise to large plaques. The patches are adherent and are removed with difficulty exposing a definite under lying abrasion *Oidium albicans* is easily demonstrable The milk spot lesions of *lichen planus* are symptomless and on close examination are seen to consist of a mosaic of small irregular plaques. Characteristic lesions can be found elsewhere on the body Mucosal lesions may occur

in association with and corresponding to the macular skin eruptions following *sulphonamides* Erosion is frequent and the resulting appearance may closely simulate the eroded mucous patch of secondary syphilis. The history of drug ingestion the brighter appearance of the skin rash and the absence of glandular enlargement should suggest the probability of drug eruption *Aphthous ulcers* occur as small, painful, superficial ulcerations with an inflammatory edge unassociated with skin or glandular manifestations. *Herpetic lesions* are commonly associated with digestive disturbances are frequently recurrent and are preceded by local irritation. A grape like cluster of small vesicles is followed by superficial ulcerations. In *erythema multiforme* the mucosal lesions commence as bullæ. After rupture a grey membrane forms over the superficial ulceration The constitutional disturbance and the associated skin lesions should suggest the diagnosis.

Condylomata lata have to be distinguished from *condylomata acuminata* or common warts and from *pemphigus vegetans* *Condylomata acuminata* may be sessile or pedunculated. There is no induration of the base the surface is frequently cauliflower-like and lacks the moist greyish top of condylomata lata. *T pallidum* cannot be demonstrated the blood Wassermann reaction is negative and there are no other evidences of syphilis. Condylomata acuminata are uninfluenced by anti-syphilitic treatment

The ultimate diagnosis of the mucosal or muco-cutaneous lesions of secondary syphilis depends on (1) the clinical suspicion of syphilis, especially when the gravity of systemic symptoms is less than one would expect from the severity of the local lesions (2) the recognition of other evidences of syphilis affecting the skin genitalia or lymphatic glands (3) the demonstration of *T pallidum* and the elicitation of the Wassermann reaction and

(4) the effect of antisyphilitic treatment in causing rapid *disappearance of the manifestations*

AFFECTIONS OF THE HAIR AND NAILS IN EARLY GENERALISED SYPHILIS

Changes affecting the hair and nails may occur during the early generalised stage of syphilis or at any later period



F 6
Syphilitic lopecia typical moth-eaten ppearance



I 6
Syphilitic alopecia simulating lopecia areata

From 5 to 10 per cent of all cases during the period of maculo-papular or papular skin rash show similar eruptions on the scalp giving rise to papular pustular *impetiginous or even rupial lesions During this period* there may be —(1) a generalised thinning of the hair or (2) syphilitic alopecia which i most marked on the back and sides of the head and gives rise to a patchy moth-eaten appearance as if the hair had been carelessly and irregularly cut close to the scalp The irregular patchy distribution of the loss of hair and the absence of exclamation mark hairs should avoid any con fusion with alopecia areata Usually complete recovery

is made under systemic treatment infrequently however a permanent baldness results



FIG. 63



FIG 64.
Syphilitic onychia

Affections of the Nails —Nail lesions may occur during the secondary period but are more common during the stage of late generalised syphilis -

(1) A *brittle condition* of the nail develops with loss of lustre The free border becomes notched or serrated. In some cases the brittleness may be associated with hyper trophic thickening

(2) There may be *pitting* of the dorsal surface the pits commencing as small whitish areas on the dorsum of the nail which when removed leave blackened rough depressions in the nail plate.

(3) *Symptomless exfoliation* of the entire nail may occur

(4) *Papular* or *pustular* lesions of the nail bed are first seen as small red patches varying in diameter from 2 to 7 mm under the normal transparent nail. The colour gradually changes to yellow the overlying nail becomes thin and crumbles away leaving a gap Usually only one nail is involved but the lesions may be multiple

(5) *Paronychia* begins as a redness and swelling round the nail bed pain being less marked than in pyogenic infection. As the condition progresses the skin breaks down giving rise to a chronic granulomatous horse-shoe shaped ulcer Extension of the process at the matrix may cause exfoliation of the nail. Syphilitic paronychia commonly results in permanent deformity of the affected nails or infrequently in their permanent absence

(6) In late generalised syphilis symmetrically distributed *spoon shaped* nails are infrequently seen and are pathognomonic

CHAPTER IV

THE TREATMENT OF EARLY SYPHILIS

THE objects of treatment of early syphilis are (1) to render the lesions rapidly non-contagious thus preventing immediate or remote risks to others and (2) to effect complete eradication of the infection in the shortest possible time so avoiding the dangers of later tertiary manifestations in the individual. Early syphilis is the vulnerable stage there is evidence that adequate treatment will cure early syphilis—the criteria of cure being absence of subsequent clinical or serological signs and symptoms of the disease non-infection of the marital partner procreation of healthy children and finally the cause of death is in no way attributable to the antecedent syphilis. On the other hand there is evidence suggesting that inadequate treatment in the early stages either from underdosage of the curative drugs or from irregularity in their administration predisposes to the later crippling cardiovascular nervous system or visceral manifestations.

Treatment may conveniently be considered under the following headings —General treatment local treatment and specific treatment

General Treatment.—It is of the utmost importance to maintain the general health of the patient The life should be carefully regulated overwork and worry should be avoided, and regular exercise with sufficiency of sleep insisted upon. The diet should be adequate especially in protein and carbohydrates but plain. Regulation of the bowels should be secured. Anæmia seborrhœa or eczema if present should be treated on general medical

principles. Alcohol and sexual intercourse must be prohibited. The use of tobacco is not absolutely contraindicated but in cases with lesions of the mouth or throat it should be used in strict moderation.

Local Treatment.—Pending diagnosis no antiseptics should be applied to the suspected lesion. Saline foments and the rubbing in of powdered sulphur control pyogenic infection and do not prevent the demonstration of *T. pallidum*. In cases of gross infection sulphonamides should be administered: these have no effect on the spirochaete and by rapidly controlling sepsis may actually facilitate its demonstration. After the diagnosis of syphilis has been established 33 per cent. calomel ointment or a dusting powder of equal parts of calomel and calamine should be applied to genital sores or condylomata. If necessary the lesions should first be cleansed with mild antiseptic, *e.g.* eusol, 1 : 10 000 solution of biniodide of mercury or 1/100 carbolic lotion. Subpreputial sores if not otherwise accessible should be treated with copious subpreputial irrigations of 1/8 000 potassium permanganate. Dorsal slitting, V-excision of the prepuce or complete circumcision may be required if symptoms persist despite irrigation and specific treatment. Mouth lesions should be treated with gargles, *e.g.* potassium chlorate, alum and borax, or peroxide of hydrogen. Chancres of the lip or moist papules in the nasolabial angle should be treated with 15 per cent. ammoniated mercury ointment. Skin manifestations and adenitis in general require no treatment. If there is a tendency to moistness in any area calomel dusting powder should be applied.

Specific Treatment.—The drugs used in the treatment of syphilis in order of therapeutic potency are (1) the organic arsenicals, penicillin, (2) bismuth preparations, (3) mercurials, and (4) iodides.

The *organic arsenical compounds* can be classified —

(1) Trivalent.	(3) Pentavalent.	(4) Bismuth-Arsenical Compounds.
Arsphenamines ("606") Arsphenamine diglucoside (Stabilarsan) N o r ph n mi ("9 4") Sulpharsphenamines. (2) Mapharside Neo-Halarsine.	Tryparsone (Tryparsamide) Acetarsol. Di thyl m e-acetarsol (Acetylarsan)	Trivalent: Sulpharsphenamin Bismuth (Bismarsen) Pentavalent: Bismuth Acetarsol (Bistovol) Tryparsone Bismuth (Bisarsamide)

The term arsphenamine is frequently employed as generic name to denote members of the arsphenamine neoarsphenamine or sulpharsphenamine groups The terms (nov)arsenobenzol, (nov)arsenobenzene, 606 and 9 4 are also similarly employed

The various trade brands of these drugs, their mode of administration and dosage for adults are —

Drug	Arsenic Per cent	Administration	Adult Dose	Indication.
Trivalent Arsenicals. *Arsphenamine* (Arsenobenzene Arsenobenzol, 606 ") Diarsenol (A. & H.) Kharsivan (B.W.) Salvarsan (Bayer)	3	Intravenous. Weekly intervals	0·30 to 0·5 gm. (0·07 to 0· gm. per 5 lbs body weight)	P m y secondary tertiary syphilis, including neuro-syphilis.
Arsphenamine Diglucoside— Stabilarsan (Boots)		Intra n weekly or twice weekly (given n-trated solution I k rsph am ines)	0·30 to 0·90 gm. (Issued in 50% glucose solution)	Do

See Note on page 7

Drug	*Arsenic Per cent*	*Administration*	*Adult Dose*	*Indication*
Neoarsphenamine (N varsenobenzol) (Novarsenobenzene 9 4 ?) Evarsan (Evans) Neokharsivan (B W) Neosalvarsan (Bayer) Novarsan (A & H) N A B (M & B) Novostab (Boots)		I t weekly or twice weekly	0-30 t 00 gm	P m y secondary tertiary syphilis, i d g neuro yphil
Sulpharsphenamine (S lpharsenobenzene) Kharsulphan (B W) Metarsenobillon (M & B) Myosalvarsan (Bayer) Sulfarsenol (Modern Pharmacals) Sulphostab (Boots)	9 5	I tram scula (once or twice weekly)	3 t 60 gm	All t ges of yphil bov when m t medication is impossible
O ophenars ne hydrochlorid Mapharside (M pharsen) (I D)	n	I tra nous	4 t of gm	All st ges of yphil s, ex cluding neuro-syphilis
Oxophenarsine tartrate Neo Halarsine (M & B)	5	I tr enous	of t 09 gm	Do
Pentavalent Arsenicals.				
Tryparsamide (Tryparsol) Tryparsamide (M & B)		I t enou (tra m sc la)	t 3 gm	Neuro syphilis
Acetarsol (Acetarsone) Kharophen (B W) Orarsan (Boots) Spirocid (Bayer) Stovarsol (M & B)		Oral	4 t 6 tablet of 5 gm da h	When other therapy not ailable
Dieth l m l etar sone— Acetylarsan (M & B)	5	I tramuscular (t ic weekly)	5 3 cc sol tion	When intra en-ous therapy is impracticable

Drug	Per cent Arsenic	Administration.	Adult Dose	Indication
Arsenic Bismuth Compounds.				
Trivalent— *Sulpharsphenamine-Bismuth—* Bismarsen (Abbott). 3 5% bismuth	13	Intramuscular	0-1 t gm alternate days for 3 doses then gm twice weekly [illegible] 20 injections	When intravenous therapy is impracticable
Pentavalent— *Bismuth Arsenal—* Bistovol (M & B) 37-40% bismuth	4 5	Intramuscular (deep subcutaneous)	Adult dose 0-3 gm (3 c) weekly	Do
Tryparsamide Bismuth— B [illegible] (B m th Tryparsamide) (M & B)		Intramuscular	0-1 t 0-25 gm (5) twice weekly	Neurosyphilis when tryparsamide is contraindicated or after long continued tryparsamide treatment

Note —A. & H Allen & Hanbury London W
Abbott Abbott Laboratories Perivale Middlesex
B D H British Drug Houses, N 1
B W Burroughs, Wellcome & Co London E C
Bayer Bayer Products Ltd., London, W C
Boots Boots Pure Drug Co Nottingham
Evans Evans, Lescher & Webb Liverpool
M & B Pharmaceutical Specialities (May & Baker) Ltd., Dagenham
P D Parke Davis & Co London W 1

The arsphenamine group of drugs is now seldom used in this country on account of its greater toxicity and because of the greater convenience of administration of the neoarsphenamines.

Neoarsphenamine is a yellowish hygroscopic easily

Drug	*Arsenic Per cent*	*Adm is tration*	*Ad lt Dose*	*I d cat on*
N oarsphenamn (N varsenobenzol) (Novarsenobenzene 9 4) Evarsan (Evans) Neokharsiva (B W) Neosalvarsan (Bayer) Novarsan (A & H) N A B (M & B) Novostab (Boot)	9	I tr ou weekly or twice weekly	0·30 t 00 gm	I m) secondary ter tiary syphilis, I d I g neuro phils
Sulpharsphenam (Sulpharsenobenzen) Kharsulphan (B W) Metarsenobillon (M & B) Myosalvarsa (Bayer) Sulfarsenol (Modern Pharmacal) S lphostab (Boot)	5	I tramuscula (nce or twic weekl)	3 t 60 gm	All sta es of yph l abov ben re t medication impossible
O aphenarsine h dro kloride Mapharside (Maphar sen) (P D)	30	I tra enous	04 t 06 gm	All t ges of syphilis, lod g neuro syph is
O phenars t rtrate Neo-Halarsine (M & B)	5	I tra enous	06 t 09 gm	Do
Pentavalent Arsenicals. *Tryparsam* (Tryparsol) Tryparsamide (M & B)	5	I t enous (inta m sc lar)	t 3 gm	Neuro phils
A etarsol (Acetarsone) Kharophen (B W) Orarsan (Boots) Spirocid (Bayer) Sto arsol (M & B)		Oral	4 t t blets f 5 m dai	When other therapy is not lable
Diethyl m l etar sone— Acetylarsa (M & B)	5	I tram sc l (t ic eekl)	5 3 solution	When tra en ou therapy is impracticable

Drug	Per cent Arsenic	Admi is-tration	Adult Dose	Indication
Arsenic Bismuth Compounds.				
Trivalent— *Sulpharsphenamine Bismuth—* Bismarsen (Abbott) 3 5% bismuth	5	Intramuscular	o· to o·2 gm lternat days for 3 doses then o· gm t ice eekly 1 t ro jection	When intraven ous therapy is impracticable
Pentavalent— *Bismuth Acetarsol—* Bistov 1 (M & B) 37–4 % bismuth	4 5	I tramuscula (deep subcutaneous)	Adult dose o·3 gm (3) eekly	Do.
Tri partose Bism th— B m d (B m th Tryparsam ide) (M & B)		I tramuscular	o· to o·25 gm (2–3) twice eekly	N ro-syphili ben tryparsamide is contra di ted or after long continued tryparsamid t eat ment.

Not —A & H Allen & Ha bury London, W
Abbott Abbott Laboratories, Perivale Middlesex
B D H British Drug Houses, N
B W Burroughs, Wellcome & Co London E C
Bayer Bayer Products, Ltd London, W C
Boots Boots Pure Drug Co Nottingham
E ns Evans, Lescher & Webb, Liverpool.
M & B Pharmaceutical Specialities (May & Baker) Ltd Dagenham
P D Parke Da is & Co London W

The arsphenamine group of drugs is now seldom used in this country on account of its greater toxicity and because f the greater convenience of administration of the neoarsphenamines.

Neoarsphenamine is a yellowish hygroscopic easily

water-soluble powder which is rapidly oxidised on exposure to the air becoming highly toxic. It is ampouled in inert gas or in vacuo and before issue for use has to conform to certain biological standards for therapeutic activity and low toxicity Certain additional precautions must be observed in its administration.

(1) *Testing of ampoule* —The contents of the ampoule must be inspected to make certain that there is no colour change indicating oxidation In cases of doubt comparison should be made with other ampoules of the same batch of drug The earliest sign of oxidation is a change of colour from yellow to a brownish red or cayenne pepper appearance Minute cracks or recent flaws may be detected by immersing the ampoule in spirit for a few minutes The spirit rapidly penetrates to the interior causing the drug to adhere to the glass Any faulty ampoule should be discarded.

(2) *Solution of the drug* —The solvents commonly employed for the neoarsphenamines are doubly distilled water 10 per cent sodium iodide or colloidal iodine solution (C I N S Crookes's) 10 per cent sodium or calcium thiosulphate or 20 per cent glucose 10 to 20 c c. of the chosen vehicle should be drawn into a syringe the ampoule is opened and completely filled from the syringe A piece of sterile filter paper is placed over the opening in the ampoule held in position by the thumb and the contents completely dissolved by gentle agitation giving a clear yellowish solution free from any solid particles. The contents of the ampoule are then sucked up into the syringe and the needle attached ready for injection

(3) *Prior to injection* the patient should have fasted for two hours and should abstain from a heavy meal for at least two hours after injections Glucose ℥iss soda bicarb gr xx oil of lemon ♏i aqua ℥iii–iv may be given by mouth one hour before injection to increase the glycogen content of the liver The urine should be tested for the

presence of bile and albumin and the patient's weight recorded. Injection of neoarsphenamine is generally made with the patient seated in the case of nervous patients the recumbent position on a couch should be adopted.

Technique of Intravenous Injection.—After application of a tourniquet the point of the hypodermic needle is introduced into the lumen of the chosen vein (p 26) and its position confirmed after fixation of the syringe by the reflux of blood on gentle retraction of the plunger The tourniquet is now released and injection is completed slowly by gentle pressure on the piston rod. It is important that during injection the needle point should remain in the vein and not be either withdrawn or pushed through the further wall. If the patient complains of any pain or if there is any suggestion of swelling of the tissues in the region of the needle point injection should be stopped immediately and the position of the needle investigated by gentle suction or by detachment of the syringe. If there is no free ooze of blood the needle point is not in the vein it is wise to withdraw the needle and recommence the operation. After injection the patient should press on the site of the puncture with a small pad of sterile cotton wool for a few moments to prevent hæmorrhage and should rest for one hour

Dosage of Neoarsphenamines.—The commencing dose of neoarsphenamines depends on the stage of syphilis and on the age weight and general condition of the patient In early syphilis an initial dose of 0 45 gm may safely be given in the adult male and 0 30 gm in the female. If there is no immediate intolerance subsequent dosage is 0·60 gm and 0·45 gm. respectively In selected individuals a dose of 0·75 to 0·90 gm. may be well tolerated in the male or 0·60 gm in the female The interval between individual doses is from five to seven days a full unit course of treatment comprising 4 5 gm. to 7·0 gm of neoarsphenamine in ten weeks.

Sulpharsphenamines.—In contrast to the 606 and 914 group of drugs which give rise to marked local reaction the sulpharsphenamines give rise to little pain stiffness or local necrosis on deep subcutaneous or intramuscular injection On this account they are employed when intravenous medication is impracticable. After inspection and testing the ampoule is opened and the dose is dissolved in from 1 to 3 c.c. of the solvent. Sterile double-distilled water is commonly used but in the case of sensitive patients a vehicle containing a local analgesic, *e g* chlorbutol gr 1/26 ethocaine hydrochloride gr ½ glucose (55 per cent. w/v) to 1 c.c may be substituted The clear yellowish solution is drawn up into a 5 c c. syringe.

Technique of Intramuscular Injection.—The preparation of the patient is as for arsphenamine administration. The site generally chosen for intramuscular or deep subcutaneous injection of sulpharsphenamine (or bismuth) is the upper outer gluteal quadrant Injection may be made with the patient lying prone on a couch or standing erect. In the latter case it is important to secure relaxation of the muscles at the site into which injection is to be made. The patient should stand with the toes slightly turned in the weight of the body is transferred to one leg and the opposite knee is bent slightly relaxing the gluteal muscles on that side The skin over the site of injection is sterilised with spirit or tincture of iodine The palm of one hand is laid flat on the buttock below the proposed site of injection and by downward pressure tautens the skin. A stout intramuscular needle 2 to 2½ inches long is held by its mount between the forefinger and thumb the tip of the middle finger resting on the shaft close to the mount and is stabbed smartly into the chosen site Care should be taken that while the insertion is sufficiently deep to reach the muscular layer the iliac bone is not struck Should this occur the needle must be withdrawn half an inch The introduction of the needle should be painless

pain indicates transfixation of a nerve in which case the needle should be almost completely withdrawn and re-inserted at a slightly different angle. It is important to wait for a few moments to make certain that the point has not punctured a blood vessel If this has occurred partial withdrawal and re-insertion is necessary If there is no ooze of blood the needle is steadied between the thumb and the first two fingers of the left hand the syringe is attached, and the dose of drug injected. The syringe and needle are then rotated once or twice and rapidly withdrawn. Deep rotary massage of the area of injection should now be made with a large pad of cotton wool wrapped in linen to distribute the drug through the tissues and prevent subsequent pain or tenderness It is advisable to instruct patients undergoing intramuscular therapy to massage the site of injection for a few minutes each day with the hands placed flat on the buttocks. Successive injections should be given on alternate sides and the site should be varied slightly on each occasion. *The dosage* for adults of the sulpharsphenamines varies from 0 30 to 0·60 gm. the principles of administration are similar to those of neo-arsphenamines.

Mapharside and Neo-Halarsine.—In recent years mapharside has come into prominence in the treatment of syphilis. It is a trivalent arsenical which is the hydrochloride of the substance frequently referred to as arsenoxide and now officially known as oxophenarsine. This is thought to be the active substance to which arsphenamine and neo-arsphenamine are converted in the body The dosage varies from 0·04 gm. to 0·06 gm given intravenously in 10 c.c distilled water Neo-Halarsine is the tartrate of oxophenarsine, the corresponding doses being 0·06 gm. and 0·09 gm. given in 6 c c. and 9 c c. respectively of distilled water It is claimed that toxic reactions are less frequent after the use of arsenoxide than after the arsphenamines

Bismuth preparations take second place in the treatment of syphilis They can be administered only intramuscularly and have a less rapid but more prolonged action than that of the arsenicals. There is considerable variation in the rapidity of absorption and excretion and in the local pain and tissue damage following injection depending to a great extent on the compound used and the vehicle. In general the water soluble and oil soluble salts are rapidly absorbed and excreted while the metal in fine dispersion or in the colloidal state and the insoluble metallic salts are more slowly absorbed and excreted The various bismuth preparations commonly used in this country are —

Drug	Bismuth Content Calculated in Metallic Bismuth per	Administration	Dose
1 **Water Soluble Preparations.**			
Thiobismol (P D) (S d m B m th Thioglycollate 37% B)	0·074	I tra muscular	0· 4 8 gm twice c. eekly
Metallic or Colloidal Suspension.			
( ) *I Isotonic Glucose Solution*—			
Bisglucol (M & B)	0· g		0· 4 gm once eekly
Bismostab (Boots)	0· g		
Hypol d B m th (B & W)	g		
(b) *I Creocamph Base*—			
Bicreol (B & W)	5 g		3–2·7 c. 4 gm onc weekly
3 **Water Insoluble Salts.**			
(a) *I aqueous suspension*			
Bismoxyl (B D.H) (Bism th oxychloride and chloretone in distilled w ter 0· gm. per c.	0·08 g		2– 1 3–3 c c. 0 4 gm once weekly according to preparations.
Bismuth Oxychloride (B.W) (in Isotonic Saline) 0· gm per c.c.	0·08		

Drug	Bismuth Content Calculated as Metallic Bismuth per c.c.	Administration.	Dose
Chlorostab (Boots) Bismuth oxychloride (in Isotonic Glucose 0·6 or 0·10 gm of salt per c.c.)	0·18 or 0·6 gm.	Intra muscular	0·2 – 0·4 gm 5–3 c.c. once weekly according to preparation.
5) I Oily Suspension			
Bismutol (M. & B.) (Bismuth Salicylate, 0· gm. per)	3 gm		
Bismuth Salicylate (Martindale) (0· gm per)	0·06 g		
Oil Soluble Preparations.			
Neo Cardyl (M. & B.) (Bismuth Betylthiolaurate)	5 g		twice weekly
Stabismol (Boots) (Bismuth -Carboxylcyclohexylacetate)	0· g		c. twice weekly
Bismuth-Iodine-Quinine.			
Preparations in Oily Suspension.			
Quinostab (Boots)			
Rubyl (M. & B.)	04 g		twice weekly
Oral.			
Sobisminol Mass (Lilly) (Capsules of 0·75 gm containing 50 mgm Bismuth)			6–9 capsules daily. When other means of medication are impracticable. Of value in manifest tertiary skin lesions.
Inunction.			
Sopenasol Bismuth Cream (Blythswood) †			
Combinations with Organic Arsenicals.	(See pp. 65, 67.)		

Eli Lilly & Co., Basingstoke
† Blythswood Chemical Co. Glasgow

The bismuthials are generally supplied in individual-dose ampoules or in phials of from 5 to 30 c.c Prior to ad ministration the greatest care must be taken to ensure an even distribution of the insoluble suspensions by thorough shaking of the container or in the case of suspensions in a creocamph base by heating in a water bath to over 20 C. and stirring with a sterile glass rod. Every precaution must be taken to prevent bacterial contamination The bismuth preparation is drawn into a syringe through a wide-bore cannula a fresh needle being used to complete the intra muscular injection The site and technique of administra tion are the same as for sulpharsphenamine.

Bismuth seldom gives rise to toxic sequelæ. It is important that before administration the patient s teeth and gums should be inspected and any necessary dental treat ment carried out The teeth should be cleaned with a soft tooth brush at least twice daily with common salt ʒi to a tumblerful of water Some degree of pigmentation of the gum margin is inevitable but in cases of gross dental sepsis ulceration may seriously interfere with the further administration of bismuth

The **dosage** for adults calculated in terms of bismuth metal is from 0·074 to 0 148 gm. of water soluble bismuth compound (*i.e* 1 to 2 c c of the preparation) twice weekly for suspensions of metallic bismuth and insoluble salts 0·2 to 0 4 gm. (varying from 1 to 5 c c. according to the preparation used) once weekly The oil soluble compounds are given in dosage of 0·05 to 0 1 gm (1 to 2 c c) twice weekly

In general if rapidity of action is required the water soluble or oil soluble preparations should be employed for slower and more continuous action water insoluble preparations are used.

Mercury Preparations.—The use of mercury in the treatment of syphilis has been superseded to a great

extent by more therapeutically potent bismuth preparations. Mercury has however a definite place as an alternative in cases of intolerance to bismuth and in the therapy of the cardio-vascular and visceral lesions of tertiary syphilis. The various modes of administration are —

(a) *Orally*.—Liquor hydrarg perchlor or liquor hydrarg biniodid. may be given in doses of ʒss. to ʒi three times daily or tab hydrarg c cret. grs. iii to grs. iv daily The disadvantage of oral administration is the liability to gastro-intestinal irritation and in many cases it is necessary to combine tincture of the perchloride of iron with the fluid preparations or pulv ipecac co gr i with the solid preparations to act as an intestinal astringent. The oral administration of mercury should in general be reserved for patients for whom other methods of administration are not available. Administration should be continued for three weeks followed by a rest of one week and continuing thus as long as is necessary

(b) *Inunction* is seldom practised in this country to be efficient it requires a specially trained mercurial rubber The preparation used is unguentum hydrarg ʒi is rubbed into a different area of the body each day the limbs abdomen and back in rotation avoiding hairy areas and the flexor aspects The time taken for each inunction is from 15 to 20 minutes A course comprises daily treatments for eight weeks after which a rest period of four weeks is permitted. During the period of treatment it is important to attend to the hygiene of the skin and to keep a careful watch for salivation or other oral signs of intolerance

(c) *Intravenous injection* of mercurials may be made when a rapid effect is desired as for example in the therapeutic test One to two c.c of 1 per cent. cyanide of mercury may be injected daily or on alternate days. A careful watch must be kept for signs of gastro-intestinal, renal,

or oral intolerance. Alternatively Crookes's collosol mercury sulphide may be given intravenously in doses of 1 to 5 c.c. once weekly or 1 to 3 c.c. twice weekly. Little intolerance follows the use of this drug.

(*d*) *Intramuscular Injection.*—Intramuscular and intravenous injections are the most certain methods of securing adequate dosage of mercury. The preparations for intramuscular injection are metallic mercury in a creocamph base, *e.g.* Squire's cream or Lambkin's cream, or mercury salicylate in a creocamph base or with chloretone. The collosol mercury sulphide used for intravenous medication may also be given intramuscularly.

The technique of injection of the drug and the preparation of the patient are the same as for sulpharsphenamine or bismuth administration. The dosage calculated in terms of metallic mercury should be gr. 1 weekly.

Iodides.—The iodides have no direct action on the spirochæte; their value lies in the ability to prevent the deposition or cause the absorption of fibrous tissue. They should therefore be exhibited in any stage of syphilis when it is desired to open up fibrotic lesions and render the spirochæte more accessible to the arsenicals. Iodides are particularly indicated in the treatment of early syphilis whenever there is induration of the individual lesions. Orally potassium iodide may be administered in doses of grs. xx to grs. lx three times daily. Intravenously a 10 per cent. solution of sodium iodide may be given in doses of 10 to 50 c.c. or collosol iodine (C.I.N.S. Crookes's) in doses of 5 to 20 c.c. weekly.

INTOLERANCE AND TOXIC REACTIONS TO ARSPHENAMINE TREATMENT

Reactions following the administration of arsenicals may be local or general and may occur early or late in the course of treatment. There are certain relative or absolute

contra-indications to the use of arsphenamines e g advanced cardio-vascular lesions gross hepatic, renal, or visceral disease tuberculosis and alcoholism. Each case must be judged on its individual merits and assessment made after careful examination of the patient as to whether the possible advantages of arsphenamine treatment outweigh the risks involved. In general, where there is the possibility of specific causation of the symptoms rapid improvement should follow a very modified dosage of 914.

Local reactions are most commonly due to faulty technique of administration Extravenous injection of arsphenamine causes an intense local inflammatory reaction which often goes on to necrosis and sloughing of the tissues. The observation of the precautions already recommended to make certain that the needle is within the lumen of the vein and is kept there during injection should prevent this occurrence. Where, however paravenous injection has occurred the affected area should be infiltrated with 10 per cent. sodium thiosulphate solution or normal saline. Hot fomentations should be frequently applied. If however these measures do not prevent the onset of suppuration or if the swelling becomes very great surgical incision is indicated

Venous Thrombosis.—Thrombosis may follow intravenous injection the vein becoming palpable as a firm thrombotic cord There may be slight pain or a feeling of stiffness on movement of the elbow joint No treatment is generally required and the symptoms disappear in from ten days to three weeks time.

General reactions to the arsphenamines may be —

(1) *Immediate* —Occurring during immediately after or within twenty four hours of injection of the drug

(2) *Late* —Varying in time of onset from a few days to several months after the commencement of treatment

During the administration of arsphenamine the patient may complain of the taste or smell of garlic. Nausea, vomiting and palpitation may occur These sequelæ may be prevented by slow injection of a dilute solution of the drug Injection shock may result from too rapid injection the patient feels faint the pupils dilate there is a marked fall in blood pressure and a state of collapse follows

Millan's Nitritoid Crisis, or Vaso-Dilator Reaction.—During or immediately after injection the patient experiences respiratory and cardiac distress the face becomes flushed the lips and tongue swollen and the conjunctivæ red and injected. Vomiting and diarrhœa may occur The pupils dilate and a state of pulseless collapse with loss of consciousness follows This condition although alarming is seldom fatal and the symptoms are rapidly controlled by the subcutaneous injection of one-half to one c c. of adrenalin solution.

Prevention is by careful preparation of the patient before injection by the oral administration of calcium gluconate grs. xx three times daily or by pre-medication one-half hour before injection with atropine sulphate gr Above all the extremely slow injection of a more dilute solution of the drug should be practised

The Jarisch Herxheimer Reaction.—Within a few hours of arsphenamine injection a flare up of the symptoms and signs occurs, frequently accompanied by rigors headache and rise of temperature The skin rash becomes more vivid or in other cases patients who previously showed no cutaneous manifestations present an intense secondary eruption The exacerbation is temporary the temperature drops to normal within twelve hours and marked fading of the skin rash is noted in twenty-four or forty-eight hours. In certain situations *e g* when there are lesions involving the larynx the local swelling associated with

the reaction may give rise to danger of asphyxia or in the case of an interstitial keratitis exacerbation of pain may be so great as to necessitate application of ice bags and the administration of morphia

Serous Apoplexy (*Hæmorrhagic Encephalitis or Arsenical Encephalopathy*) generally occurs within twenty-four to forty-eight hours after the first second or third injection or more rarely at any time later in the course of treatment The onset may be sudden and simulate acute uræmia or apoplexy More commonly however there is a gradual onset with nerve irritability headache inability concentrate and loss of memory The patient rapidly to becomes stuporose, develops convulsions and dies within twenty four to forty-eight hours.

Treatment is by venesection up to 20 ounces of blood being withdrawn by thecal drainage 20 to 50 c.c. of cerebrospinal fluid being removed by intramuscular injection of adrenalin 1 c.c. four hourly and by the intravenous injection of calcium salts or magnesium sulphate Administration of oxygen may be of value There is no known method of prevention of this condition because of its occurrence late after injection the true cause may not be recognised, especially if the patient is not known to be undergoing treatment Recovery is possible only if vigorous treatment is instituted early

Ventricular Fibrillation may occur in cases of syphilitic myocarditis. During injection the patient s face becomes ashen the pulse impalpable consciousness is lost and before any remedial measures can be taken the patient dies. This occurrence can be prevented by careful preliminary medication with mercury and iodides orally and bismuth intramuscularly before the exhibition of arsphenamine

Within twenty four hours of injection headaches rigors albuminuria diarrhœa, and vomiting may occur and may

be associated with some rise of temperature. *Urticarial or erythematous* rashes of a transient nature may occur These are due to the arsphenamine and have to be differentiated from the Herxheimer reaction from erythema of the ninth day and from the early stages of post-arsenical dermatitis.

Later reactions.—*Malaise mental depression* and *loss of weight* may occur It is important in these cases to examine the patient to exclude the possibility of any organic lesion as a contributory factor The dosage of arsphenamines or the intensity of administration may require modification Some degree of loss of weight—usually unaccompanied by symptoms—commonly occurs during a course of treatment This is generally made up during the subsequent rest period

Albuminuria may occur from the direct toxic action of the arsenicals or bismuth on the kidney Repeated estimations of the urinary albumin should be made in these cases and the effect of the injections noted If necessary complete renal function tests should be carried out Temporary discontinuation of arsphenamine or modification of subsequent dosage may be required to avoid permanent renal damage

Milian s Erythema of the Ninth Day—This is a morbilliform or scarlatiniform erythema occurring eight to ten days after the first injection of arsphenamine The erythema is self limiting and does not progress to a true post arsenical exfoliative dermatitis The condition is ushered in by malaise headache backache nausea, vomiting diarrhoea and a febrile reaction of 100 to 102 F In from twenty four to forty-eight hours a bright erythematous rash appears on the trunk and arms gradually spreading over the entire body Oedema especially of the eyelids ankles and feet occurs and is associated with a marked albuminuria The blood urea and non protein

nitrogen are not raised. Erythema of the ninth day is differentiated from the Herxheimer reaction by its delayed onset, by the character of the rash and by the persistence of temperature for over twelve hours and from the early stages of exfoliative arsphenamine dermatitis by the tendency towards spontaneous cure. There is no untoward reaction on continuation of arsphenamine therapy

Treatment is to a great extent symptomatic. Large doses of salicylates or of potassium citrate may afford marked relief but are not infrequently ineffective. Intravenous injection of calcium or sodium thiosulphate is of more constant value especially when combined with the administration of Vitamin C mgm 50 to 100 t.d.s.

More serious manifestations of intolerance may occur jaundice exfoliative dermatitis and blood dyscrasia.

Jaundice.—Post therapeutic jaundice most frequently occurs towards or subsequent to the end of the first course of arsenicals after the possibilities of specific causation have been eliminated. Considerable difference of opinion exists as to the nature of post-arsenical jaundice and its relationship to catarrhal jaundice. The possibilities are (1) a toxic hepatitis due to arsphenamine (2) an intercurrent catarrhal jaundice precipitated in patients harbouring the causal virus by the added toxic effect of the arsenicals on the liver or (3) a virus infection transmitted by imperfectly sterilised syringes contaminated with serum.

In a number of cases no symptoms precede the onset of clinical icterus in others general malaise joint pains nausea vomiting, mental depression and slight temperature may persist for seven to ten days prior to the skin discoloration. In the former group there is marked enlargement of the liver and often of the spleen this is frequently absent in the symptomatic cases. The severity of the attack may vary from the mildest jaundice

persisting only a few days to a rapidly progressive liver atrophy (acute or subacute liver necrosis) the average duration being from two to four weeks.

Prevention.—There is no certain means of preventing the occurrence of post therapeutic jaundice elimination of dental or other focal sepsis avoidance of constipation abstention from alcohol and a diet adequate in protein *carbohydrates calcium sulphur and Vitamins, C and* B_1 are the principal measures. Prior to injection of an arsenical the urine should be tested with Ehrlich s reagent To 5 c c. of urine two drops of a 3 per cent solution of paradimethylamminobenzaldehyde in 50 per cent hydrochloric acid is added The presence of a pathological amount of urobilogen is shown by the development within a few minutes of a deep red colour A positive Erhlich test contra indicates the administration of arsphenamine

Treatment.—Injection of arsenicals and bismuth must immediately be stopped. The patient should if possible be hospitalised or at least confined to bed in a warm room in order to minimise as far as possible the strain on the metabolic activities of the liver A fat free high protein high carbohydrate diet should be given. Action of the bowels is secured by saline purgatives Glucose is given in large quantities by mouth or intravenously in 20 per cent solution (20 to 50 c c. daily) Vitamin C should be exhibited in all cases 300 mgm daily by mouth for three days then 100 mgm. daily until the jaundice is clear 25 mgm. of Vitamin B_1 should be administered parenterally daily for the first three days, then 5 to 10 mgm daily by mouth.

In mild cases a mixture —

Sodii bicarb grs. viiss.
Sodii salicyl grs. viiss
Sodii thiosulph grs xv
Tr nucis. vom ♏ viiss.
Pulv rhei. gr i
Aq menth pip ad. ℥ss.

is of value. In more severe cases intravenous injection of calcium thiosulphate (6 c.c. to 9 c.c. of a 10 per cent solution daily for three or four days then on alternate days and at gradually increasing intervals according to the progress of the individual case) controls the mental depression relieves pruritus and shortens the duration of the icterus

After the jaundice has cleared treatment should be recommenced with bismuth or mercury and iodides. The decision as to when arsphenamine therapy may safely be resumed depends on the severity and duration of the icterus. In mild and transient cases where the icterus has persisted for one week or less a period of six weeks is sufficient. In the more severe cases three to six months should elapse before further arsenical therapy is considered. Small doses should be given at first and the patient carefully watched for untoward effects. Cases in which any degree of liver atrophy has occurred should receive no further arsphenamine therapy

Dermatitis.—Post-arsenical dermatitis may occur early or late in the course of arsphenamine administration and is predisposed to by pre-existing dermatoses *e g* seborrhoea by oral or other focal sepsis, or by the abuse of alcohol. Premonitory symptoms frequently precede the occurrence of the rash Itching of the back of the hands and dorsum of the feet persisting 24 to 48 hours, is noticed after arsphenamine injection. If the arsenicals are not withheld this pruritus becomes more marked and persistent after each injection and finally becomes generalised. A morbilliform, scarlatiniform or papular erythema appears at first localised to the back of the hands but rapidly spreading over the entire body At this stage there is generally slight subcutaneous oedema. Vesiculation may occur Within five to ten days exfoliation sets in weeping fissures appear in the flexures. Scaling is profuse the underlying skin being smooth dry and

shining or moist and matt and of a dull livid red colour Excoriation and secondary infection may follow scratching In the more severe cases the hair and nails are shed The patient is toxic and miserable the temperature rises to 100 to 104 F oedema of the extremities and of the face and eyelids becomes marked Constipation is the rule in the early stages later a persistent diarrhoea may develop and be associated with ulcerative colitis Conjunctivitis, broncho-laryngeal catarrh and albuminuria of varying severity frequently occur There may be concomitant jaundice and peripheral neuritis.

Prevention —As in jaundice there are no certain preventive measures the same dietary precautions treatment of pre-existing dermatoses and elimination of septic foci must be rigorously observed Careful observation of the patient must be made during the course of arsphenamine administration to detect dermal intolerance in its earliest stage Treatment in the early erythematous stage will arrest the progress. Many patients however do not appreciate the urgency of the condition and do not report until the vesicular or exfoliative stage supervenes

Treatment —The patient should be admitted to hospital without delay Arsphenamine and bismuth administration must immediately be discontinued The main danger of exfoliative dermatitis is the occurrence of bronchopneumonia. If this complication can be prevented the patient should make a complete recovery Calcium (or sodium) thiosulphate (which should be given four hourly for the first three days) and Vitamin C should be administered in arsenical jaundice In the early stage local applications of lin calamine are of value in the later stages when exfoliation is profuse daily mucilage baths relieve the itching and remove the scales One to three pounds of bran or oatmeal and if available an equal quantity of tarch are placed in a muslin bag

suspended in a large pan of boiling water simmered for one to two hours and then allowed to cool. A bath is filled with water at 100 F sufficient to cover the patient s body The mucilaginous contents of the pan are now added. The patient enters the bath and uses the muslin bag as a sponge to clear the skin as far as possible from



Fig 65
Exfoliative stage of arsenical dermatitis

scales. The temperature of the bath must not be allowed to fall below 98 F and the patient should not remain immersed longer than 15 minutes. Drying is accomplished by wrapping in a large warm soft towel gently pressed over the various parts of the body after which an oily application should be made e g olive oil, liquid paraffin or for small areas castor oil

After the exfoliative stage has passed colloidal baths should be reduced in frequency and oily applications, *e.g* ung zinc oxide and castor oil equal parts continued. When the skin has nearly returned to normal the oily applications may be discontinued and a dusting powder



FIG. 66.
Exfoliati stage f arsenical dermatitis

(½ per cent ac salicyl in talc) substituted Conjunctivitis should be treated by lavage with boric lotion and subsequent instillation of liquid paraffin or castor oil. Persistent diarrhoea indicates probable intestinal ulceration and should be treated by starch and opium enemata. If dehydration is marked restoration of the lost fluids should be accomplished by the administration of glucose solution orally or intravenously

The course of exfoliative dermatitis may take from ten days to ten weeks. Pigmentary changes may follow arsphenamine dermatitis: these fail to respond to any treatment. The Wassermann reaction, if previously positive may become negative during the course of a dermatitis remaining negative for a period varying from a few weeks to several months and later becoming positive again.

In general the occurrence of an arsenical dermatitis permanently contra indicates the further administration of arsphenamines. In certain cases, e.g. in young adults it may be permissible to test the tolerance of the patient to the pentavalent arsenicals e.g. acetylarsan, or to the trivalent oxophenarsines or in the event of neuro-syphilis being detected at a later date tryparsamide. The decision as to whether it is justifiable to administer these drugs must depend on the urgency of the individual case. A patch test should be carried out: if negative small doses of the chosen drug are given and the effects carefully watched. The patient must be made aware of the possibilities and advised to report at the earliest sign of any untoward reaction.

Blood Dyscrasia occurs late in the course of treatment of syphilis often after irregular arsphenamine administration from progressive damage to the bone marrow leading successively to (1) *thrombocytopenia*—decrease in the number of blood platelets to under 40 000 being followed by subcutaneous purpuric patches and hæmorrhages from the mucous membranes (2) *granulocy-topenia* characterised by hæmorrhages and sloughing of the oro-pharyngeal tissues often associated with a brawny œdema of the neck (agranulocytic angina) and (3) *aplastic anæmia*.

Thrombocytopenic purpura may occur within a few hours to a week after the injection of an arsenical: granulocytopenia and aplastic anæmia may not become apparent

for several weeks after the last injection In milder cases the occurrence of purpura may be the first indication of hæmopoietic damage in more severe cases premonitory symptoms occur Fever malaise pain in the joints and at the ends of the long bones, and giddiness may precede the onset of purpura. The clinical picture varies from a few scattered purpuric spots to severe skin mucosal, and conjunctival hæmorrhages hæmaturia hæmatemesis and melæna and necrotic stomatitis. Jaundice and exfoliative dermatitis may occur in association with blood dyscrasia.

The blood count shows a decrease in red cells normal or low colour index, leucopenia with relative lymphocytosis and reduction of granulocytes and marked fall in the number of blood platelets A progressive decrease of all the cellular elements is of the gravest significance

Treatment—Hospitalisation of the patient and repeated blood examinations are essential. The less severe cases of asymptomatic purpura may be controlled by the administration of calcium thiosulphate intravenously and Vitamin C orally Occasionally Vitamin P in moderate doses seems to be of value In more severe cases these measures should be supplemented by daily intramuscular injection of 10 c c. pentose nucleotide until definite improvement is shown by the appearance of young polymorphonuclear cells and reticulocytes in the blood films. Repeated blood transfusion is used for those cases failing to react to pentose nucleotide but seems of doubtful value.

The subsequent antispecific treatment of the patient should be continued without arsphenamines. Penicillin bismuthials, or intravenous colloidal mercury sulphide should be employed. The pentavalent arsenicals or mapharside may be tolerated but their administration should be reserved for cases of special urgency and the effects of each injection controlled by blood examinations.

Oxophenarsine and Pentavalent Arsenicals.—Reactions

following the use of arsenoxides and pentavalent arsenicals are more rare, but are similar to those mentioned above. The special precautions required in the case of tryparsamide administration will be dealt with under neuro-syphilis.

Bismuth.—Following the first few injections, local tenderness and stiffness may be noted the muscles however rapidly acquire a tolerance to bismuth injection. Painful local infiltrations of the tissues or even abscess formation may result from errors in the technique of intramuscular injection It is important that all such precautions as sterility of the syringe needle and drug should be observed The needle when inserted into the tissues should be left for a moment or two to make certain that the point has not punctured a blood vessel. If this has occurred, the needle should be withdrawn an inch and reinserted in a slightly different direction. Intravenous injection may be followed by a severe nitritoid crisis, while intra-arterial injection may cause embolic gangrene of the skin. Painful infiltrations result from the injection being deposited in the subcutaneous fat too close to the skin or from injection into the deep fascia. Painful infiltration should be treated by the application of heat and by gentle massage with the flat of the hand. Abscess formation necessitating surgical incision is rare.

The commonest sequel of continued bismuth administration is the occurrence of a blue line on the gums. Bismuth is deposited in the form of insoluble sulphide in the tissues the common sites being the region of the lower incisors and molars. Dental sepsis and tartar formation are predisposing causes, and the severity of bismuth stomatitis depends on the degree of dental sepsis. The gums become spongy and reddened and the free border shows a blue-black pigmentation. Tenderness is complained of there is increased salivation a metallic taste in the mouth and the odour of the breath becomes foetid.

Later deep ulceration may occur with grey sloughing tissue covering the ulcers. The pigmentation may extend to the apposed mucous membrane of the lips or cheeks. Prevention is by early dental care and by cleansing the teeth and gums twice daily with a good dentifrice or with common salt one teaspoonful to a tumblerful of water The gums should be inspected weekly for evidence of a bismuth line A slight degree with firm gums and no



Fig 67
Well-marked bismuth line on gum



Fig 68
Bismuth pigmentation on inner aspect of lip.

symptoms does not contra indicate the continuance of treatment but a careful watch must be kept for any more serious involvement A gargle of —

Potassium chlorate ʒiii
Alum sulphate ʒii
Glycerini ac boric ʒiii.
Aqua ad ℥viii.

℥ss. to a half tumblerful of water is of value enabling the patient to continue bismuth injections

More severe pigmentation or the onset of ulceration necessitates withdrawal of the drug or the substitution of mercury *The gums should be thoroughly cleansed with* peroxide of hydrogen, and painted over with a weak tincture of iodine Calcium thiosulphate injections intra venously relieve local pain but have no effect on the

duration of the condition. The length of time of cessation of bismuth treatment in mild or severe cases may vary from four to fourteen weeks.

Albuminuria and *Nephritis* may follow bismuth administration. If albuminuria is noted on routine examination on more than one occasion the drug should immediately be stopped and the renal function of the patient thoroughly investigated. In general the albuminuria is associated with the presence of casts and blood the condition clears up rapidly on withdrawal of the drug

Of gastro-intestinal symptoms, diarrhoea is the most common manifestation. This may be controlled if severe by a starch and opium enema. If less severe however regulation of the dosage of bismuth or the administration of some astringent, *e.g* Dover's powder may be required.

Malaise loss of weight and *nervous symptoms* may follow prolonged administration from the cumulative effect of the drug Cessation of the drug the administration of tonics and in the case of neuritis, Vitamin B_1 are indicated. Dermatitis which may go on to exfoliation may occur but is seldom met with

Mercury in the dosage at present administered seldom gives *rise to any sequelæ Stomatitis and other symptoms* may occur as in bismuth administration

Iodides.—Headache coryza lachrymation, and infrequently skin eruptions follow the administration of iodides. Relief follows withdrawal of the drug

COURSES OF TREATMENT

The schemes of treatment employed for early syphilis fall into one of three main categories —

(1) Routine long-term arseno-bismuth therapy
(2) Intensive arseno-bismuth therapy

(3) Penicillin now almost invariably combined with arseno-bismuth therapy

Since penicillin has become available in a form suitable for out patient administration routine treatment is reserved for those cases who cannot receive injections more than once weekly intensive treatment is usually carried out in hospital but may be applied to out-patients attending three or four times weekly while daily injections of penicillin are necessary during the period of administration of this drug

Routine, long-term treatment —There are two generally accepted schemes namely the *concurrent intermittent* scheme which is almost universally employed in this country and which consists of an adequate number of unit courses (of concurrent arsphenamine and bismuth injections) separated by rest intervals and the *alternating continuous* scheme in which no rest intervals are allowed treatment consisting of alternating series of arsenical and bismuth injections

It must be emphasised that while courses of treatment suitable for the majority of patients in any of the various stages of the disease may be mapped out as a general guide it is essential that each individual case be considered separately and the intensity and duration of treatment modified or augmented to secure for the patient the greatest prospect of cure with the minimum risk of untoward sequelæ.

Concurrent intermittent therapy may conveniently be considered in periods of approximately three months this time covering the administration of a unit course and the subsequent rest period. The *unit courses* advocated for young otherwise healthy adult males or females are shown on p 93

When the diagnosis of syphilis has been confirmed by the demonstration of *T pallidum* in the suspected lesion

U rr Courses.

Week		Neoarsphenamine (I V) or Sulpharsphenamine (I.M)		[illegible] Bismuth Suspension of insoluble metal or metallic salt (I.M.)	or Liposoluble Bismuth twice weekly (I M)	or Mercury Suspension of metal or metallic salt (I M.)
		Males.	*Female*			
	1st day and	0·45 gm	0·45 gm	0·20 gm	0·06 gm.	gr 1
	4th day	0·30 gm	0·30 gm	0·20 gm	06 gm.	gr 1
		60 gm.	0·45 gm	20—0·30 gm	0·06 gm. 0 06 gm.	gr 1
3		60 gm.	0·45 gm.	0·20—0·3 gm	0·06 gm. 0·06 gm.	gr 1
4		0·60 gm	0·45 gm.	0·20—0 30 gm	0·06 gm 06 gm	gr
5		0·60 gm	45 gm	0·20—0 30 gm.	06 gm 06 gm.	gr 1
6		60 gm.	0·45 gm	0·20—0·30 gm	0·06 gm 0·06 gm	gr
7		0·60 gm	0·45 gm	20—0·30 gm	0·06 gm 0·06 gm.	gr
1		0·60 gm	0·45 gm	0·20—0·30 gm.	0·06 gm. 0·06 gm	gr 1
9		60 gm	45 gm	0·20—0·30 gm	0·06 gm 06 gm.	gr
		60 gm	0·45 gm	0·20—0·30 gm	0·06 gm 06 gm.	gr 1
	Tot	6 5 gm	4·80 gm	20—3· 0 gm.	20 gm.	gr. xl

I V = intravenous injection.
I M = intramuscular injection.

and the initial blood Wassermann report is negative, this test should invariably be repeated five to ten days after the first dose of arsphenamine has been administered. This acts as a provocative frequently converting the serological reaction to positive. The provocative Wassermann reaction is of importance in the assessment of the minimum amount of treatment in early cases.

Iodides are specially indicated and should be given orally (grs. xxx t. or q d.s.) if any indurative lesions are present.

Rest Periods.—An interval of two weeks should be allowed between the termination of the first unit course and the commencement of the second. Rest periods between *subsequent courses should be four weeks. At the* end of each rest period the patient should be examined clinically and blood Wassermann or other serological tests carried out.

In the female patient of average weight an individual dose of over 0.45 gm. neoarsphenamine may not be tolerated; large well-built women who show no reaction to the smaller dose are often found to tolerate without ill effects the dosage recommended for males.

The time duration of treatment and the weight of drugs necessary for the adequate treatment of a patient depend to a great extent on the clinical stage to which the disease has progressed before therapy is instituted. The clinical classification and the treatment advocated can be summarised:—

	Number of Unit Courses Advocated.
Primary Syphilis.	
Sero-negative (*T. pall* + W. R. negative—Provocative W. R. negative)	3
Sero-positive (*T. pall* + W. R. positive or Provocative W. R. positive)	4
Early Generalised Syphilis.	
(Muco-cutaneous eruption—W. R. positive)	5

W.R.=Wassermann reaction.

The clinical manifestations of early syphilis disappear rapidly under dual therapy and in the majority of cases the serological test, if positive at the start of treatment

are reduced to negative by the end of the first unit course. If however the serological reactions remain positive until after the termination of the second (or a later) unit course, then additional courses of treatment must be administered so that not less than four are completed after the first negative blood Wassermann reaction has been obtained.

The detailed scheme for treatment of early syphilis is —

		Neo-arsphenamine	*Bismuth*
st–9th week	First Unit Course —	6·5 gm. (M.) 4·80 gm. (F.)	2–3 gm.
oth– th week	Rest Period		
rth– oth week.	Clinical and serological examination — second unit course —	6·5 gm. (M.) 4·80 gm. (F.)	3 gm.
		Neo-arsphenamine	*Bismuth*
1st 24th week	Rest Period		
5th–33rd week.	Clinical and serological examination—third unit course —	6·5 gm. (M.) 4·80 gm. (F.)	2–3 gm.
		End of treatment of sero-negative primary syphilis — surveillance commences.	
34th 37th week	Rest Period		
38th 46th week.	Clinical and serological examination — fourth unit course —	6·5 gm. (M.) 4·80 gm. (F.)	2–3 gm.
		End of treatment of sero-positive primary syphilis — surveillance commences.	

47th–50th week.	Rest Period			
51st–59th week.	*Clinical and serological examination—fifth unit course*	—	6·15 gm. (M.) 4·80 gm. (F.)	2–3 gm
				End of treatment of [illegible] syphilis—surveillance commences

M = male patient.
F = female patient.

Observation after completion of Treatment.—After treatment has been completed according to schedule the patient enters upon a period of surveillance of at least one year preferably two years or even longer During this time clinical and serological examinations should be repeated at three monthly intervals On at least two occasions during the observation period a provocative dose of 0 45 gm of neoarsphenamine should be given one week prior to the taking of blood for serological examination to reactivate and obtain serological indication of any possible latent infection

The systems to which it is necessary to pay great attention in examination are the central nervous system and the cardio-vascular system. Routine clinical examinations must be supplemented during the second year of observation by the examination of the cerebro-spinal fluid and radiological examination of the heart and aorta.

If the blood serological tests remain negative during the two years probationary period and if no abnormalities are found in the central nervous or cardio-vascular systems clinically or on special examination the patient may safely be discharged as cured

Women however should be advised to receive treatment during any and every subsequent pregnancy as an absolute assurance of procreating healthy children

Alternating continuous treatment, as the term implies indicates alternating series of injections of neoarsphenamine or bismuth given alone. A ten weeks course of neoarsphenamine (dosage as in unit course table) is followed by bismuth injections twice weekly for six weeks. This sequence is continued until a weight of neoarsphenamine and bismuth equivalent to that in three to five unit courses has been administered

Mapharside and Neo-Halarsine.—Either the concurrent intermittent or the alternating continuous plan of treatment may be employed. In the concurrent method the patient receives fifteen weekly injections of the arsenical and bismuth or mercury followed by a rest period of two weeks. A minimum of three such courses is recommended for early sero-positive syphilis additional courses being required for more advanced infections. In alternating continuous treatment an eight weeks dosage of mapharside is alternated with six weeks administration of bismuth five such sequences being recommended for sero-positive primary syphilis.

The **subsequent treatment** of cases **complicated** by treatment reactions or **toxic sequelæ** may present some difficulty The clinician is desirous of exhibiting an adequate weight dosage of drugs within a reasonable time period to ensure for the patient greatest possible chance of cure On the other hand there is the danger that in patients who have previously shown intolerance more serious reactions may follow normal dosage. In the case of minor reactions to treatment a change from one brand of arsphenamine to another alteration of the vehicle from distilled water to glucose or thiosulphate solution greater dilution of the drug and extremely slow injection may prevent further incidents. In other cases the dosage may have to be modified to suit the patient s tolerance If none of these measures succeed it is necessary to substitute

intramuscular sulpharsphenamine or acetylarsan or one of the other therapeutically less active compounds for the arsphenamines

In these cases requiring modification of dosage or alteration of the drug the period of treatment and observation must be correspondingly lengthened.

Intensive Arsenotherapy —Intensive short term in-patient treatment of early syphilis has been advocated. At first a *five-day course* of neoarsphenamine totalling 4·0 to 4 5 gm. was employed, the drug being dissolved in 5 per cent dextrose solution and given intravenously by continuous drip 0·90 gm daily in six units of 0·15 gm. in from eight to ten hours.

The high incidence of toxic reactions led to the trial of arsenoxide (mapharside) and to the substitution of multiple injections for the continuous drip The scheme adopted was —

Day	*8 a.m*	*noon*	*4 p m*	*8 p m*	*midnight*	M pharside
	0·04	0·06	0·06	0·06	0·06	1 2 gm
3, 4 5	06	0·06	0·06	06	06	
					Total	4 8 gm
7	*Blood Wassermann reaction*					
						or dosage of 06 or 09 gm Neo-Halarsine

This form of treatment is only applicable to fit young adults suffering from early syphilis For twenty four hours prior to treatment the patient is confined to bed the bowels are regulated and 5 per cent glucose solution is given liberally by mouth and continued throughout the course of treatment The diet should be plain but high in protein and carbohydrates. During the injection period the urine should be tested twice daily by Ehrlich s reagent for urobilinogen. The occurrence of a positive test or of a temperature reaction persisting for more than 24 hours are indications for interrupting the treatment

Five-day treatment is followed by a high incidence of toxic sequelæ of the same nature as in routine therapy. While the ultimate end results have not as yet been fully evaluated a follow up over several years shows a cure rate of approximately 80 per cent.

The intensive therapy of human syphilis has been modified following the observation that the time period within which the curative dosage of arsenoxide must be administered to be effective in experimental animal infection can be varied within wide limits. The curative dosage of mapharside for human syphilis has been estimated to lie between 20 and 30 mg. per kilogram body weight administered in the maximum time period of eight weeks. The shorter and more intensive a scheme of treatment the lower is the margin of safety and the greater the incidence of toxic sequelæ. A longer course of treatment, equally effective without entailing a higher individual or total dosage of the arsenical, decreases the risk of complications and makes intensive treatment more widely applicable. The schemes of intensive treatment now being widely used are the 20-day course and the 7 week course.

Twenty-day course.—A weight dosage of 1 mg. mapharside or 1½ mg. neo-halarsine per kilogram body weight is administered daily for twenty days; eight to ten injections of 0·2 gm. bismuth are given in the same time period. The patient should be hospitalised but need not be strictly confined to bed. The diet must be high in carbohydrates and protein (minimum 250 gm.) and should include at least one pint of milk daily. The urine should be tested twice daily with Ehrlich's solution and a complete blood-count should be repeated twice-weekly. The patient's temperature should be taken four hourly. Primary fever following the first injection is of no significance; secondary fever occurring at any

time between the fifth and fifteenth days may be due to drug sensitisation or may herald the onset of more serious complications—encephalitis hepatitis or blood dyscrasia. Treatment should immediately be suspended. In the absence of localising symptoms or signs indicating more serious organic damage the temperature reaction is probably due to drug sensitisation. When the fever has been mild, i e less than 102 F desensitisation may be attempted after the patient has been afebrile for two or three days. A commencing dose of 6 mg mapharside or 9 mg neo-halarsine is given intravenously A slight temperature reaction may follow but this settles to normal in twenty four hours or less. The dose of arsenoxide should be doubled daily until the maximum is reached and the course of twenty injections completed. In cases in which the temperature reaction is more severe i.e. 103 F or over desensitisation should not be commenced until the temperature has been normal for five days. The same sequence is followed the initial dose should however be 0·06 mg mapharside, or 0·09 mg neo-halarsine The majority of patients showing secondary fever complete treatment without further incident those in whom secondary fever persistently recurs or in whom frank complications develop should be treated along the lines previously described

A quantitative Wassermann reaction should be carried out twice weekly during the course of intensive treatment and is of value in prognosis. The most favourable case is that which remains sero-negative throughout Serologically positive cases showing a progressive fall in Wasserman titre have also a good outlook. An initial rise in titre is of bad prognostic import and patients in whom this occurs should be most carefully observed for clinical or serological relapse. When indicated a second intensive course may safely be undertaken

Seven week course.—In this course the total dosage of arsenoxide and bismuth is similar to that employed in the twenty-one day course the only difference being that injections are given thrice weekly instead of daily The same precautions should be observed.

Penicillin has been shown to possess spirochæticidal properties and has been applied to the treatment of early syphilis, causing healing of the primary lesion disappearance of the secondary manifestations and reversal of the positive serological reactions. The original dosage of 2,400 000 Oxford units of penicillin in seven-and-a half days advised for the treatment of early syphilis has proved to be too low and observations on experimental animal infection suggest that the curative dosage is probably in the region of 10 000,000 Oxford units and that a synergic action exists between penicillin and the arsenicals. It is now recognised that penicillin has not a fixed chemical formula but that the product consists of a number of fractions, the proportion of which varies according to the method of preparation certain of these fractions are relatively ineffective against syphilis. The current trend in treatment is therefore to increase the dosage of the non toxic penicillin to the maximum and to combine this therapy with arseno-bismuth administration At first penicillin could only be given in saline solution necessitating hospitalisation and injections at three-hourly intervals, day and night to ensure an effective tissue concentration. The introduction of penicillin emulsions in 2 to 5 per cent. beeswax in arachis oil or ethyl oleate has made this therapy possible for ambulant patients a single dose maintaining an effective titre for from 12 to 24 hours

Penicillin in the pure state is a white powder but as usually supplied has a yellowish tinge. It is available in sterile ampoules containing from 100 000 to 1 000,000

Oxford units of the sodium or calcium salt or in vials of 10 to 20 c.c. of oil wax emulsion containing 125 000 or 200 000 units per c.c. Before use the penicillin powder is dissolved in sterile saline solution and the appropriate dose injected intramuscularly or intravenously In the treatment of syphilis and of gonorrhœa the intramuscular route is favoured because of the slower absorption and longer therapeutic effect When oil wax emulsion is employed the vial should be heated to 45–50 C. if necessary to reduce the viscidity and the required dose withdrawn into a dry warm syringe through a large-bore needle intramuscular injection is completed with the minimum of delay using a finer needle Prolonged or over heating of the emulsion should be avoided as this leads to destruction of the penicillin

No serious toxic manifestations have followed the use of penicillin. Discomfort or pain of varying severity at the site of injection may be experienced especially after repeated injections of oil wax emulsion Herxheimer reactions occur in twenty five per cent. of cases of early syphilis and may necessitate a reduced dosage of penicillin for twenty-four hours. Temperature reactions which may reach 102 or 104 F not infrequently follow massive dosage (300 000 to 800 000 units) of oil wax emulsion in the treatment of gonorrhœa or syphilis the temperature falls to normal in twelve to sixteen hours. In women temporary disturbances of menstrual rhythm may be found notably premenstrual or menstrual dysmenorrhœa premature onset of the periods and increased loss.

The schemes of combined penicillin-arseno-bismuth treatment at present in use are designed to administer an adequate dosage of the drugs in the safe minimum time period —

Penicillin —7·5 to 10 million units in 15 days For

in-patients three-hourly injection of saline solution of penicillin (63,500 to 83,400 unit approximately) are given day and night For out patients a single injection of oil-wax emulsion (5 to 7 million units) is administered daily

plus

Arseno-bismuth therapy commencing on fourth day of penicillin administration —

(*a*) 20-day intensive neohalarsine bismuth course (p 99) (In-patients.)

Or

(*b*) 7 week neohalarsine-bismuth course (p 101) (Out patients.)

Or

(*c*) one unit course of neoarsphenamine and bismuth (p 93) (Out patients.)

Or

(*d*) A six to eight weeks course of twice-weekly injections of neoarsphenamine and bismuth. For males 0·45 gm. is given on each occasion along with 0·2 gm. bismuth for women the weekly dosage of arsenic should be 0·45 gm. + 0·3 gm. the bismuth dosage remaining unaltered.

The end results of combined penicillin-arseno-bismuth treatment of early syphilis have not yet been fully evaluated. The individual patient must be advised as to the absolute necessity for the most careful observation over a minimum period of two and preferably four years.

The cerebro-spinal fluid should be examined ten to fourteen days after completion of treatment and clinical and serological investigations should be carried out at monthly intervals during the first year apart from these variations surveillance is as already indicated on p. 96

CHAPTER V

LATE GENERALISED SYPHILIS (TERTIARY SYPHILIS)

MUCO-CUTANEOUS MANIFESTATIONS OF LATE GENERALISED SYPHILIS

IN the absence of diagnosis and treatment the manifestations of florid secondary syphilis run their course in from three to nine months and finally disappear spontaneously The defensive mechanism of the body has eliminated the spirochaete from the blood stream and from many of the tissues or organs of the body Complete eradication of the parasite is however not accomplished, and a state of equilibrium is reached between the tissues and the infecting organism, the spirochaetes being confined to a number of residual foci The attainment of this stage of equilibrium leads to an asymptomatic period which may vary in length from a few months up to fifty years or more

So long as residual foci of spirochaetes persist in the body there may be (1) slowly progressive insidious damage to the tissues involved by these rests (e g aorta liver bone marrow central nervous system) and (2) recurrent waves of spirochaetaemia following disturbance from trauma or other cause of the tissue-parasite equilibrium.

The late manifestations of syphilis may conveniently be considered according to the systems involved under the following headings —

(1) Skin mucosal bone muscle joint lesions
(2) Cardio-vascular and visceral lesions
(3) Neuro-syphilis
(4) Asymptomatic infection

While lesions affecting a number of tissues or organs may appear simultaneously it is more usual to find only one system involved. In view however of the gravity of cardio-vascular and neuro-syphilis it is of the utmost importance to make a set routine of clinical and special investigation of these systems in every case of late syphilis coming under observation.

Muco-cutaneous Manifestations of Late Syphilis.—The earlier the recurrence of spirochætæmia the more likelihood there is of widespread and symmetrical lesions often corresponding to the pigmentary or papular secondary eruption and healing without scarring or tissue destruction. Mucous patches moist papules and condylomata lata are not infrequently met with The later the manifestations appear the greater is the tendency to asymmetrical distribution and to solitary lesions or lesions localised to one area of the body

The muco-cutaneous manifestations of late syphilis may be classified —

(1) Nodular (*a*) non-ulcerative
(*b*) ulcerative
(2) Squamous
(3) Gummatous (gummous)

Nodular Cutaneous Syphilides* commence as lesions in the corium increasing slowly in size and often taking from one to three months to reach a diameter varying

* The gumma is the essential lesion of tertiary syphilis and is characterised histologically by a diffuse or localised infiltration of small round cells, plasma cells, hyperplastic fibroblasts and, not infrequently giant cells The blood vessels are increased in number and show endothelial proliferation and perivascular infiltration leading to partial or complete occlusion Areas of caseation or necrosis occur

The nodular cutaneous syphilide is therefore a localised or diffuse gummatous infiltration of the skin which does not break down, or in which intact and ulcerated nodules occur in varying ratio at the same time

from one-quarter to one inch The sites commonly affected are the nose forehead chin neck back buttocks and outer aspect of the thighs

The individual lesions are circular in outline and may be solitary or grouped in circular serpiginous,



F 60

Nodula cutaneous syphilide tw years fter primary nfection Solitary od les t hair margin la forms t left The form entre show peripher l bead ng and central healing

or kidney-shaped patches They can be palpated as firm elastic sharply circumscribed nodul s involving the entire thickness of the skin The surface i of a reddish brown or coppery colour and is u ually smooth and non-scaly Fine desquamation may however occur The nodules may remain localised and persist without apparent change for a year or even longer more

commonly however central necrosis or peripheral spread occurs.

Central necrosis gives rise to deep circular punched out ulcers with sharp edges and a base covered with crusts or gummy exudate Healing is by non-contractile atrophic scar tissue. Peripheral spread may occur in solitary lesions or in groups of nodular lesions giving rise



FIG. 70

Nodular cutaneous syphilide of temple following blow some three months previously Proliferati phase well marked T small areas of ulceration



FIG 71

Nodular cutaneous eruption volving foot and ankle. Duration fiv years Proliferati phase well marked with many areas of ulceration.

to a slowly advancing continuous or broken narrow or broad border of circular or serpiginous outline. The area of skin over which the spread has taken place may be apparently unaltered or may show atrophic squamous cicatricial crustaceous or ulcerative changes. Alteration of pigmentation increase or decrease is not infrequent in those cases in which otherwise apparently normal skin is left

The advancing edge of the lesion varies in colour from

pinkish-brown to red-copper is slightly raised and scaly and invariably shows palpable infiltration of the entire thickness of the skin and nodule formation The nodules



Fig 7

Widespread nodular cutaneous syphilide of scaly type Pigmentary changes and white scars of healed lesions are marked Three years duration

may be scanty and widely separated or may be close together and resemble a chain of beads The larger the nodules and the more closely they are set together the greater is the possibility of ulceration and subsequent scar

tissue formation While the rate of spread is slow taking from three to twelve months to advance six inches wide areas of skin may be involved before the patient seeks advice The process is usually unattended by any general upset

Diagnosis —Nodular cutaneous syphilides have to be differentiated from other conditions giving rise to nodular



FIG. 73.
Serpiginous, psoriasiform, nodular cutaneous syphilide

or raised lesions in the skin *e g* urticaria eczematides tuberculosis sebaceous cysts lipomata fibromata The spreading circinate or serpiginous lesions have to be differentiated from seborrhoea, psoriasis ringworm rosacea lupus erythematosus, lupus vulgaris mycosis fungoides leprosy and epithelioma The asymptomatic, slowly progressive sharply defined indurated nodular lesions of syphilis occurring in circles or segments of

circles the punched-out ulceration and atrophic non-contractile scars should suggest the possible diagnosis. The main points in differentiation between the nodular



I 74
Nod lar taneous syphilide f right hypogastrium Proliferati phase not marked Ulcerative phase predominant.

cutaneous syphilide and the commoner diseases with which it may be confused are summarised on page 111

Ringworm is a superficial lesion lacking the indurated border and nodules of a serpiginous syphilide. Minute vesicles are present at the advancing edge The fungus is easily demonstrable microscopically

Nodular Cutaneous Syphilide	*Psoriasis*	*Lupus Vulgaris*	*Epithelioma.*
Occurs in older people	Occurs t any ge	Occurs in young subjects.	Occurs tor after middle ge
I d d l lesions circular and occur in circinate or serpiginous pattern.	I n d I d l lesions are cir cular—may form gyrate patterns.	Lupus nodules have p p l jelly colour and appearance	Epithelioma is usually solitary and commences as superficial w t y t growth. T l giectases may be present.
Progress is slow	Course is chronic m y p t throughout life	Course is haracterised by ex treme chronicity	Progress is slow
Colour is red d b br or red-copper with scant friable, d b w scales	Patches are f reddish colour d with bundant silvery scales Removal f the scale gi es typical capillary haemorrhage.	Colour is rod dish-pink.	Colour may show little alteration in early stages.
I d rat on f activ areas of l marked firm and lastic and in volves the entire thickness f the skin	I d ti l absent	The lesions f lupus are soft and not indur ted	The growth feels stony hard
Punched out lcers ith cir lar or crescen- ic edge occu Crusting is not ncommon	Ulceration never occurs	Ul h ndermined and irregular edges	Central lcer t oc rs, lea ing raw granular easily bleedi g base The edge of the lcer is rolled and pearly Crusting may occur
Atrophic thin supple firml healed scars fol low the ulcera tion	Scar forma ion never occ rs	Dense hard, in lastic scars are left, often with act ve nod les their substance	There is no tendency to heal spontaneously

Nodular Cutaneous Syphilide	*Psoriasis*	*Lupus Vulgaris*	*Epithelioma*
May heal without treatment	Serological evidences of syphilis absent		
Other clinical or serological evidences of syphilis present.		The diagnosis of tubercle may be confirmed by evidences of tuberculosis elsewhere by guinea pig inoculation, or culture of the tubercle bacilli.	The diagnosis is confirmed by biopsy



Fig 75

Serpiginous nodular cutaneous syphilide of thigh Duration three years Commenced as small nodule spreading peripherally Note wide spread of edge—nodulation not marked Residual area of activity in the apparently normal skin left after the passage of the lesion

Mycosis fungoides is characterised by marked pruritus and in the early stages by multiple chronic erythematous infiltrated scaly skin plaques of circular or gyrate shape These lesions may persist for many years before the more serious development of tumours occurs These vary in

size and shape and are of a deep red colour Softening occurs giving rise to deep fungating ulcers.

In *Lupus Erythematosus* there is superficial inflam



Fig 76.



F 77

Ulcerat nod la utaneous yphilide of knee, showing ffect of six eeks treatment N te pical non-contracted, trophic sil ery scars

mation of the skin, consisting of reddish infiltrated plaques covered by adherent scales. The follicles of the involved r as re patulous and contain epidermal plugs which are often adherent to the overlying scales. The condition pre d peripherally healing in the centre leaving atrophic

skin superficial slightly depressed scars and telangiectases. Ulceration never occurs

Squamous Syphilides (*Palmar or Plantar Syphilides*) — The occurrence of nodular cutaneous syphilides on the palms or soles gives rise to well-defined diffuse or localised scaling lesions of circular outline and dull red colour. Ulceration or fissuring never occurs. The squamous syphilides have to be differentiated from the manifestations of eczema, psoriasis and ringworm. Acute palmar



Fig 78

Nodular cutaneous syphilide of right naso-labial fold and upper lip. Infiltration of skin with small areas of ulceration. These were the only cutaneous manifestations of syphilis in this case

eczema is characterised by vesicles; in chronic eczema scaling is marked, the skin is markedly thickened and fissured and there is a marked tendency to involvement of the interdigital folds.

Gummatous Syphilides.—While the nodular cutaneous syphilides are intracutaneous gummata, the true gumma commences as a small firm painless circumscribed nodule in the subcutaneous or deeper structures, *e g* the periosteum of the long bones. This nodule gradually increases in size until a diameter of from one-half to two inches is



Fig. 79.
Squamous syphilides are nodular cutaneous syphilides affecting the palms or soles



Fig. 80.
Subcutaneous gumma of right cheek with commencing involvement of skin



Fig. 81.
Gummous ulceration of triceps and region of elbow showing deep scars and muscle deformity

reached Central softening occurs the gumma becomes adherent to the skin and breaks down forming an ulcer with vertical punched-out edges sharply defined circular or kidney-shaped border and a base covered with gummy exudate a wash-leather or boiled fish slough The skin surrounding the ulcer may be normal in appearance or may show a reddish or purplish discoloration Crusting may occur giving rise to a rupial appearance The gumma is usually of solitary occurrence not infrequently however clusters of gummata occur in the same area giving rise to polycyclic skin ulcerations. The tissue destruction following gummatous ulceration is often considerable. Gummatous syphilides may occur anywhere on the body the commonest sites being the upper part of the lower leg the face trunk arms and scalp.

Gummata must be differentiated before ulceration from the various conditions giving rise to subcutaneous nodules—sebaceous cysts lipomata fibromata and infrequently sarcomata from erythema nodosum erythema induratum (Bazin s disease) and after ulceration from tuberculous ulcers malignant disease varicose ulcers actinomycosis etc

The diagnosis of non ulcerated subcutaneous gumma from fibromata lipomata and sebaceous cysts depends on its occurrence later in life its more rapid onset and increase in size and its tendency to central softening and involvement of the skin Other evidences of syphilis may be present on the skin or mucous membranes and the serological reactions are almost invariably positive

Erythema nodosum is more common in the female adolescent and is accompanied by some degree of constitutional disturbance and joint pains Groups of oval swellings with their long axis parallel t th at f th limbs



FIG. 82
Typical punched out gummous ulceration of leg



FIG. 83
Diffuse gummous ulceration of chin.

appear on the extensor aspect of the legs and arms below the knees and elbows. The colour is at first bright red and the lesions are firm, tense and tender. Later they become soft and semi-fluctuant and of a dusky purplish tint; suppuration never occurs. There is a marked tendency to recurrence. The constitutional disturbance is often a symptom of tuberculosis in its early stage.

Erythema induratum (*Bazin's disease*) most commonly



FIG. 84.
Gummous destruction of ala nasi.



FIG. 85.
Widespread facial gummous destruction ("syphilitic lupus").

affects young females between the ages of twenty and thirty. The disease affects only the legs, usually the lower half of the calf posteriorly. Multiple indolent symmetrical nodules develop below the skin which takes on a purplish-red lividity. The nodules increase in size and central ulceration occurs, giving rise to irregularly-shaped ulcers. There may be separation of sloughs. Recurrent lesions are common. Depressed white scars from previous ulceration are commonly present with active lesions in all stages in the same area of skin. The appearance may be highly suggestive of gummatous ulceration, but the

blood Wassermann reaction is negative and evidences of tuberculosis may be found elsewhere.

Varicose Ulcers frequently require to be differentiated from gummatous ulcers. The main points are —

Varicose Ulcer	*Gummatous Ulcer*
Is common in middle-aged females	Is common in middle-age males and females are equally affected.
Is associated with varicose veins.	
Commonly occurs on the lower third of the leg.	Commonly occurs on the upper third of the leg.
Is usually single.	May be single or multiple.
May be painful	Is usually painless.
The outline is frequently irregular	The outline is circular oval or kidney shaped.
The edges are rounded and undermined.	The edges are sharply punched out.
The base is angry red or grey	The base is covered with gummy exudate or wash-leather slough
Pigmentary changes surrounding the ulcer are associated with eczematous changes in the skin.	The ulcer may be surrounded by an area of pigmentation varying in colour from reddish-brown to purple
The varicose ulcer is slowly progressive there is little tendency to heal, and constant liability to break down	Gummatous ulceration frequently heals spontaneously with characteristic trophic "parchment" scars
The Wassermann reaction is usually negative (Varicose ulceration may occur in syphilitic patients)	The Wassermann reaction is almost invariably positive.
Varicose ulceration is unaffected by antispecific treatment	Gummatous ulceration heals rapidly with antispecific treatment

Malignant Disease —Gummous ulceration may be confused with rodent ulcer or with epithelioma. Rodent ulcer is much more slowly progressive than gumma, and the raised rolled stony hard edge is characteristic

Actinomycosis produces a reddish-purple diffuse hard swelling in the tissues, with multiple sinus formation and a free discharge of pus in which the streptothrix can be demonstrated The common site is in the cervico facial region The onset is insidious and the lesion is slowly

progressive. Anti-syphilitic treatment other than potassium iodide is of little value.

Late Syphilitic Lesions of the Mucous Membranes.—*Localised or diffuse infiltrations* corresponding to the nodular cutaneous syphilides may involve the mucous membranes especially those of the tongue the hard and soft palate the lips the tonsils and the pharynx. These infiltrations may remain unulcerated giving rise to sclerotic patches or may break down causing superficial ulcerations followed by flat reticulated irregular cicatrices.

Gummata may occur in the sub-mucous tissues or on the underlying periosteum or bone The hard palate is especially liable to involvement The gumma gives rise to the typical symptomless swelling followed by central softening and ulceration leading to bone necrosis and perforation of the palate

Interstitial Sclerotic Lesions commonly affect the tongue less frequently the lips or other areas of the buccal mucosa. The perivascular interstitial infiltrate gives rise to chronic interstitial glossitis which may be superficial or deep In the early stages the tongue is red swollen and glazed Later the appearance is that of a smooth glistening dull red epidermis with complete loss of the small papillæ As a result of cicatricial contracture superficial furrowing or deep fissuring of the tongue becoming more accentuated as the process continues leads to irregular lobulation distortion and fibrous contracture Lymphatic obstruction may result in macroglossia The common sequel to interstitial glossitis is *leucoplakia* which occurs characteristically on the dorsum or lateral surfaces of the tongue and on the buccal mucosa at the tooth line Leucoplakia is not necessarily a manifestation of syphilis but rather a protective tissue reaction to chronic irritation Apart from syphilis alcohol tobacco spices and dental irritation are important causal factors The prominent

symptom is local sensitiveness to hot food, or drinks, to highly spiced foods or other irritants. The early stages of



FIG. 86
Gummous ulcer of dorsum of tongue



FIG. 87
Chronic interstitial glossitis, showing loss of small papillæ



FIG. 88
Chronic interstitial glossitis showing marked fissuring and lobulation of tongue



FIG. 89
Chronic interstitial glossitis, showing marked white patches of leucoplakia

leucoplakia show slight pearling of the epithelium when well developed white thickened opal-like plaques are found

Leucoplakia has to be differentiated from the mucous patches or moist papules of early syphilis from the oral lesions of lichen planus and from thrush In the treatment of leucoplakia control of all sources of local irritation is essential. Slow symptomatic improvement follows anti-specific therapy but the local condition often remains apparently unaltered Leucoplakia must be regarded as a pre-cancerous condition and careful investigation and long-continued observation made to exclude malignant degeneration

Treatment of Late Generalised Syphilis.—Tertiary syphilis may prove serologically resistant to treatment and it is difficult to give other than a general guide. Before commencing treatment of patients showing skin bone muscle or joint lesions it is essential to exclude any serious cardio-vascular syphilis or central nervous system involvement Involvement of these systems may either necessitate modification of the dosage of drugs which it is permissible to give for the external tertiary lesions or indicate special measures primarily applicable to the treatment of the affected system. In the absence of contra indications the treatment of the manifestations of late generalised syphilis follows the scheme laid down for early syphilis.

During the first 59 weeks of treatment five unit courses of treatment are given

Subsequent to this treatment may be mapped out —

60th–63rd [illegible]eek	Rest
64th–73rd	Bism[illegible]th oil ([illegible] 3 gm [illegible]eekl[illegible]
74th–77th	Rest
78th–87th	Sixth unit course
88th–9[illegible]	Rest
[illegible]2nd [illegible]	Course [illegible]f bismuth alone
[illegible]2nd–[illegible]5th	Rest
[illegible]6th [illegible]5th	Seventh [illegible] course

The signs and symptoms in general disappear during the first or second unit course of treatment In many of

the cases, however the Wassermann reaction remains persistently positive In those cases in which the Wassermann reaction has become negative it is wise to stop treatment at the end of the 115th week the patient then being kept under three-monthly surveillance.

When the blood serology still remains positive at the end of two years treatment it is wise during the third year to continue the alternation of bismuth and arsphenamine-bismuth courses. Such cases should have a cardiovascular X ray and complete serological examination of the cerebro-spinal fluid carried out during the second year

These cases in which the Wassermann reaction remains positive (" Wassermann fast cases ") present the difficulty that while there is serological evidence of a persistent focus of *T pallidum* infection in the body there is no clinical evidence of disease The persistence of a positive Wassermann test does not imply that the disease is active or progressive or that it constitutes any immediate danger to life or good health

The Wassermann reaction may be negative in a small percentage of cases of late syphilis showing clinical manifestations When the clinical appearances are highly suggestive of syphilis the serological tests should be repeated after provocative injection of neoarsphenamine. *If the results are still negative, the therapeutic test i.e* the empirical administration of treatment should be undertaken Rapid improvement follows in cases of syphilitic ætiology

Penicillin in dosage similar to that employed for early syphilis causes rapid healing of skin lesions and reduction of the amount of Wassermann reagin in the blood. Subsequent arseno-bismuth therapy should be instituted.

CHAPTER VI

SYPHILIS OF BONES, JOINTS, MUSCLES, TENDONS AND BURSÆ

IN *early generalised (secondary) syphilis involvement* of the bones joints muscles and fascial structures may give rise to symptoms or signs. Arthralgia ostealgia or pain referred to the tendinous insertions of the muscles in the region of the larger joints may occur without demonstrable anatomical basis or in association with localised areas of tenderness These symptoms are transitory and undergo spontaneous relief as the secondary eruption fades.

In late syphilis bone and joint lesions run a slower course the symptoms are usually more severe and more *protracted and are associated with permanent changes in* the bones affected

There is no basic difference between the pathological changes underlying syphilis of bone and syphilis of other structures. The same vascular and peri vascular changes leading to localised or diffuse inflammatory granulomatous tissue or gummatous infiltration occur the later new bone formation or less frequently rarefaction is due to the specialised anatomical structure of the bony tissue attacked

The bones most commonly affected in order of fre-*quency* are the tibia, the nasal and palatal bones the cranial bones the femur the humerus and the patella

Classification.—According to the structures involved the bone manifestations of syphilis may be classified —

(1) Ostealgia (osteocopic pains)		
(2) Periostitis.		Localised
(3) Osteitis.		or
(Panosteitis or osteomyelitis)		Diffuse.
(4) Gummata.		

Ostealgia may vary in degree from a slight dull ache up to the most excruciating lancinating pains. This manifestation is usually intermittent not infrequently migratory and invariably presents periodic nocturnal exacerbations (commonly about two a.m.) of such severity as to interfere with rest. No local abnormalities are detected on clinical or X-ray examination. The absence of physical signs leads usually to a diagnosis of rheumatism, neuritis or neuralgia. The history of nocturnal exacerbation and the failure of salicylates to afford relief should lead to the suspicion of syphilis. Specific treatment is rapidly effective. Pain of similar nature is met with in cases showing definite bone changes.

In **periostitis** the changes consist at first of periosteal thickening causing tender areas. Later sub-periosteal deposition of new bone gives rise to localised osteophytes or exostoses or diffuse bony thickening. Diffuse ossifying periostitis must be differentiated from osteogenic sarcoma. In syphilis periostitic changes are seldom confined to a single bone there is increased density of the whole circumference of the shaft, and thickening giving rise to a fusiform swelling tapering off into normal tissue. In sarcoma there is infiltration only of that side of the bone from which the growth arises.

Osteitis may be *localised* or *diffuse*. In localised osteitis an initial osteosclerosis is followed by an osteoporosis which may result in pathological fracture. Diffuse osteitis invariably causes sclerotic changes leading to increased circumference length and weight of the bone

involved. Bowing replaces the natural curves. The tibia and femur are most commonly affected—giving rise in the former to the sabre blade deformity which



F 90
Early syphilitic periostitis of tibia, showing early new bone formation



F 9
Localised syphilitic periostitis of tibia showing dense new formation

however is more frequently met with in congenital syphilis. Sequestrum and sinus formation may rarely occur

Diffuse osteitis must be distinguished from osteitis deformans and from tuberculous osteitis In Paget's

disease the long bones lack the density caused by the syphilitic process and the skull is increased in size. Syphilitic osteitis may cause marked thickening of the calvarium but does not cause increase in diameter

Syphilitic *dactylitis* which occurs both in congenital and acquired syphilis commonly affects the phalanges of the fingers, less frequently the metacarpals, or the corresponding bones of the feet It is essentially a pan-osteitis and commences as a firm painless, flask-shaped bony swelling covered by normal or slightly reddened skin. Pain is absent the lesion being noticed because of mechanical interference with the movements of the hand. Syphilitic dactylitis may remain apparently stationary for several months tending ultimately to spontaneous resolution and leaving a permanently shortened phalanx Sequestrum or sinus formation is not infrequent A similar condition is met with in tuberculous infection—from which it may be distinguished by other evidences of syphilis and the result of treatment



FIG 92
Syphilitic osteo-periostitis of fibula. The changes suggest osteogenic sarcoma.



F 93
Syphilitic osteit f sk ll bowing sequestrum formation f outer table H aled nodl lar taneou lesions on heek

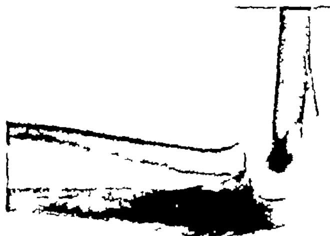


Fig 94
Syphil t osteitis of t th ll ma ked periosteal reaction

SYPHILIS OF JOINTS

The joint manifestation of syphilis may be classified —

Arthralgia Synovitis Hydrarthrosis	Secondary and tertiary syphilis.
Osteochondroarthropathy Gummous perisynovitis. Charcot s joints (in tabes dorsalis)	Late syphilis.

Arthralgia corresponding to ostealgia occurs in the early generalisation stage of the disease. The large joints—the knees, shoulders elbows wrists and ankles are most frequently involved and show no clinical or X-ray changes Arthralgia may continue for long periods in the absence of specific treatment which however rapidly terminates the symptoms.

Synovitis may be acute, subacute or chronic The acute type is more commonly met with during the period of early generalised syphilis. One or more of the large joints may be affected infrequently the smaller joints, *e g* of the fingers may alone be involved. Acute continuous pain aggravated by movement is complained of there is pronounced articular or periarticular swelling with reddening of the overlying skin and an irregular temperature which may reach 104 F X ray appearances usually show no abnormality The response to administration of arsphenamine and bismuth is prompt salicylates have no effect The subacute type is essentially similar but its course is less severe and may be followed by a chronic crepitating arthritis without effusion Radiological changes are slight Specific treatment is followed by marked improvement

Hydrarthrosis may occur in association with acute or subacute synovitis or may arise insidiously In the latter type the larger joints are more commonly affected fre-

quently the condition is polyarticular No changes apart from swelling due to the accumulation of fluid can be detected in the articular or periarticular structures on clinical or X-ray examination. Movement is limited mechanically by the effusion. The condition may tend towards spontaneous remission and recurrence.

Osteochondroarthropathy generally involves one of the *larger joints commonly* the knee or the elbow and is frequently associated with gummous osteomyelitis of the adjacent areas of long bone. The process is a combination of destructive and proliferative changes affecting the articular cartilage and underlying bone and the synovial structures giving rise to a globular distended doughy joint (white swelling) Pain may be absent in the early stages but becomes more prominent *later* The skin over the joint is pale shiny and tense. The movements of the joint are less limited than seems warranted by the extent of the lesion Ankylosis is rare unless secondary infection occurs or involvement of the skin by extension of the gummous process leads to sinus formation Osteochondroarthropathy has to be distinguished from tuberculosis. *In the former there is less destruction than in the corre*sponding type of tuberculous joint other evidences of syphilis should be looked for the Wassermann reaction is positive and specific treatment is followed by rapid im provement

Gummous Perisynovitis usually affects one of the large joints the knee being most commonly involved Synovial thickening *accompanied by effusion is noticed the joint* becoming globular The overlying skin is white thinned and shows distended veins No X-ray changes are detected. If the condition is untreated changes similar to those in osteochondroarthritis may follow The absence of bone changes and the asymptomatic course should suggest the possibility of syphilis.

Charcot's Joint (Tabetic Arthropathy) —Neurotrophic changes may affect the joints in tabes dorsalis. Usually one of the large joints, the knee hip shoulder or ankle is affected occasionally however multiple large or smaller joints may be involved In the early stages a rapid exudation occurs into the joint cavity and periarticular structures. This is followed by rapid painless articular disorganisation synovial thickening and villous forma



FIG. 95
Charcot disease of knee joint, showing marked swelling and dilatation of the superficial veins



FIG. 96
X-ray of Charcot joint, showing gross bone destruction and pathological fracture of head f tibia

tion, erosion of articular cartilage with eburnation or destruction of the underlying bone and destruction of the ligaments giving rise to a painless flail joint. The X ray appearances show gross disorganisation disappearance of cartilage and articular margins of bone and bony rarefaction. Frequently portions of osseous tissue are detached and lying free in the joint

The diagnosis is based on the rapidly progressive painless destruction of a joint without muscular wasting and on the presence of clinical and serological signs of

tabes. Syringomyelia may give rise to similar joint lesions and must be differentiated by the absence of signs of syphilis and the loss of pain and thermal sensation

Pathological fractures may occur in *tabes* *Perforating Ulcers*—Trophic ulceration not infrequently occurs in tabes the usual situation is on the sole of the foot or one of the toes The slow painless ulceration gradually extends down to the bone which may sequestrate or

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SYPHILIS OF MUSCLE

In early generalised syphilis *myalgia* corresponding to arthralgia and ostealgia may occur The pain varies in character from a constant dull ache to severe excruciations and is commonly localised towards the tendinous insertions of the muscles of the thighs and legs and less frequently in the deltoid area. Examination of the muscles shows scattered points of tenderness often of small area. There is a varying degree of interference with the function of the involved muscles generally assumed to be due to the pain.

Localised or diffuse *myositis* occurs in late syphilis and affects the biceps gastrocnemii pectorals deltoids and abdominal muscles. The onset is usually insidious the patient only experiencing slight infrequent cramps. The first sign is limitation of extension of the affected muscle the shape and consistence of the muscle are apparently unaltered but pain is marked on attempting extension As the condition progresses the muscle becomes progressively more hard and ligneous contractures become more pronounced and considerable deformity may result. The prognosis is good pain is relieved promptly by treatment and the contracture improved by remedial exercises.

Solitary or multiple *gummata* may arise in muscle The tongue triceps abdominal muscles, and sterno-mastoids are the common sites The gummatous nodule slowly increases in size undergoes central softening involves the integument and finally breaks down forming a typical gummatous ulcer Pathological rupture of a muscle may result

SYPHILIS OF THE TENDONS, TENDON SHEATHS, AND BURSÆ

Tenosynovitis.—Simple *serous tenosynovitis* may occur in secondary syphilis or later in the disease commonly

tabes. Syringomyelia may give rise to similar joint lesions and must be differentiated by the absence of signs of syphilis and the loss of pain and thermal sensation

Pathological fractures may occur in *tabes* *Perforating Ulcers*—Trophic ulceration not infrequently occurs in tabes the usual situation is on the sole of the foot or one of the toes The slow painless ulceration gradually extends down to the bone which may sequestrate or

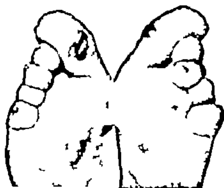


Fig 97
Perforatin g lcers tabes dorsalis

become carious. These ulcers are refractory to treatment. Similar conditions are found in diabetic peripheral neuritis

Juxta-articular Nodes are localised gummata involving the joint capsule or bursae in relation to the joint and which undergo fibrotic degeneration giving rise to a hard nodule attached to the extensor aspects of the joint capsule of the elbow knee etc A similar condition may affect the tendon sheaths. Antispecific treatment may resolve the nodes or they may prove completely refractory

skin softens and ulcerates leaving a chronic often serpiginous ulcer Sloughing of the tendon may occur

Tendons.—Single or multiple gummata may arise in the tendons as painless slowly growing nodules not inter



Gumma of quadriceps tendon Gummous ulceration of skin

fering with movement. Later involvement of the tendon sheath and the surrounding tissues may occur

Bursitis.—An indolent *serous bursitis* may occur at any time during the course of generalised syphilis. In late syphilis *gummous bursitis* may occur gradually leading to the formation of a solid bursal tumour which may later ulcerate

CHAPTER VII

CARDIO-VASCULAR SYPHILIS

SYPHILIS is fundamentally a disease of blood vessels In the chancre the underlying pathological changes are endothelial proliferation endarteritis, panarteritis perivascular infiltration with small round cells and plasma cells granulomatous tissue formation and new vessel formation The same changes are found throughout the secondary and tertiary lesions. It is not surprising therefore to find important manifestations related to the cardio-vascular system. The capillaries, veins arteries heart muscle and valves are liable to involvement during the generalised stages of the disease Infrequently symptoms or signs referable to the heart and great vessels occur during the secondary stage aortitis and aneurysm have been recorded as early as 6 to 12 weeks after infection It is however more usual to find that after an insidious onset varying in length from ten to thirty years after infection commonly in the fifth decade of life localising cardio-vascular symptoms appear

Classification of Cardio-Vascular Syphilis.—Syphilitic involvement of the heart and blood vessels may be classified —

(1) Syphilis of capillaries.
(2) Syphilis of veins.
(3) Syphilis of arteries
(4) Syphilis of aorta
(5) Syphilis of myocardium pericardium and endocardium.
(6) Hæmopoietic changes in syphilis

Syphilitic changes in capillaries have already been described.

Syphilis of Veins.—Manifestations of syphilis affecting the veins are infrequently recognised. Four forms are described —

(1) A diffuse thickening of the wall of a superficial or deep vein occurs early or late in syphilis involving the complete course of the vessel or segments of varying length The swelling may be uniform or more frequently shows irregularity in different portions. Pain is a marked feature. Thrombosis may result

(2) Localised nodular thickenings occur along the course of the vein

(3) Less marked involvement of the walls of the veins may give rise to an erythema nodosum-like eruption.

(4) A periphlebitis of chronic course leads to great thickening round distended and convoluted veins. Suppuration rarely occurs Syphilitic periphlebitis of lesser degree is not infrequently noted in association with chronic gummous leg ulcers.

Syphilitic Arteritis.—All the arteries of the body are to a greater or less degree involved in early generalised syphilis. Infrequently symptoms occur in relation to the peripheral arteries. More commonly the cerebral arteries are involved the panarteritic changes tending to vascular occlusion and the perivascular cellular infiltration giving rise to symptoms clinically suggestive of meningitis. In late syphilis gummous changes may result in fragmentation or complete destruction of the muscular coats

Syphilis of the Aorta.—Syphilitic aortitis is more common in males than in females 80 per cent. of cases being recognised in the former sex. Alcohol and heavy exertion are contributory factors in determining this differential incidence The granulomatous syphilitic degeneration commences in the vasa vasorum and the tunica media of

the aorta near the aortic valves and results in fragmentation or complete loss of elastic and muscular coats and their replacement by fibrous tissue contraction of which leads to depressed linear or stellate scars. The intima may show compensatory thickening or be apparently unaltered. The fibrous tissue gradually stretches leading progressively to aortic dilatation dilatation of the aortic ring and incompetence of the aortic valves or to varying degrees of aneurysm. According to the extent and progress of the lesions the manifestations may be classified —

(1) Simple aortitis
(2) Aortitis with aortic regurgitation.
(3) Aortitis with aneurysm formation.
(4) Aortitis with coronary artery disease.

Symptoms —In the early stages the symptoms may be vague and not directly indicative of the cardio-vascular lesion. Headache often of a throbbing character attacks of giddiness faintness on rising or stooping irritability or defects of memory may be complained of Palpitation or vague anginal pains may occur on exertion

As the underlying aortitic changes become more marked, the symptoms become more severe and localising Precordial or substernal pain of constant dull or sharp severe character occurs and may radiate to the scapula or down the arm. The facies is long drawn tired anæmic and waxy Nocturnal dyspnœa and orthopnœa and œdema of the feet may progressively occur

The earliest physical sign of aortitis is an accentuation of the aortic second sound. When aortic incompetence occurs definite clinical signs appear marked cardiac enlargement water-hammer pulse (Corrigan's pulse) capillary pulsation and increased difference between the systolic and diastolic blood pressures X ray examination shows characteristic broadening of the aorta

Aortic aneuryam is a further stage in the pathological sequence. The signs and symptoms vary according to whether the sinuses of Valsalva the ascending, transverse, or descending portion of the aortic arch are involved. Aneurysmal dilatation of the *sinuses of Valsalva* may be asymptomatic, may give rise to anginal symptoms or simply to those of the co-existing aortic incompetence.

Aneurysm of the *ascending aortic arch* may give rise to *slight or severe anginal pain, or infrequently persistent or* paroxysmal cough. The physical signs are those of an expansive pulsating tumour to the right of the sternum A systolic thrill and murmur occur over the sac the aortic second sound is accentuated or if there is incompetence is replaced by a murmur The heart is frequently displaced to the left The pupils may be unequal, and pressure on the recurrent laryngeal nerve leads to paralysis of the right vocal cord with alteration of the voice.

Aneurysm of the *transverse aortic arch* more commonly gives rise to alterations of the voice, and frequently paroxysmal bovine or brassy cough inequality of the pupils, laryngeal paralysis tracheal tug and suprasternal pulsation If the aneurysmal sac is directed downwards compression of the left bronchus may give rise to signs of bronchitis bronchiectasis collapse and carnification of the lung

Aneurysm of the *descending arch* may give rise to few symptoms other than those of pressure on the lung structures vertebræ or ribs. A pulsating tumour may be present in the left interscapular space.

Sclerosis or partial occlusion of the *coronary arteries* may occur from localised syphilitic arteritis but is not uncommonly associated with aortitis or aneurysm. Anginal attacks are frequent

Diagnosis —The possibility of syphilis should invariably be suspected in young adults developing heart disease

Vague precordial or substernal pain palpitation dyspnœa, attacks of giddiness fatigue and exhaustion on slight

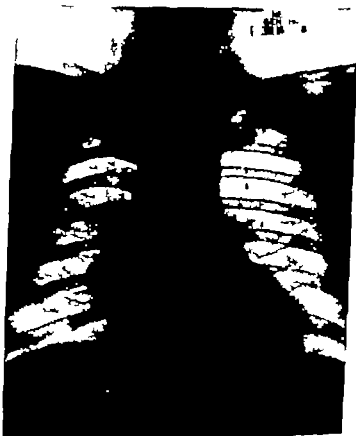


Fig. 00
Specific aortitis and aortic regurgitation. X ray shows increased width of aortic and heart shadow

exertion should lead to the examination of the cardiovascular system in known cases of syphilis. Confirmation of the clinical diagnosis is by the X ray demonstration of

an aortic dilatation or of an expansile pulsating tumour in the line of the aorta Routine X-ray examination in late



Fig
X-ray showing aortic aneurysm

syphilis frequently shows the presence of early aortic changes before clinical examination can detect them with certainty

The Wassermann reaction is invariably positive.

Prognosis.—The earlier syphilitic aortitis is detected the better is the prospect of arrest of the disease. The more advanced the physical changes the less favourable is the outlook, the expectation of life varying from six months to several years.

Syphilis of Myocardium, Pericardium, and Endocardium.—*Myocardial disturbances* may occur in the early generalisation stage of syphilis before the secondary eruption appears, the symptoms being those of a toxic myocarditis—arrhythmia, tachycardia and extrasystoles. Precordial pain may be complained of; dyspnœa and cyanosis are frequent. The diagnosis depends on the rapid onset of the cardiac symptoms in the course of a generalised syphilitic infection and is confirmed by the prompt symptomatic relief following antispecific therapy. In the late stages of syphilis, myocardial changes may follow coronary arteritis. These changes are generally interstitial fibrosis and pale degeneration of the heart muscle which may go on to fatty degeneration, atrophy, or even necrosis. The symptoms are those of a slowly progressive myocarditis. *Syphilitic endocarditis* and valvular disease may occur in association with aortitis. Pericardial changes—opalescent patches of thickening at the perforation points of the terminal arterioles have been described.

Treatment of cardio-vascular syphilis.—The *treatment* varies to some extent according to the stage of the disease in which cardio-vascular symptoms occur and with the clinical condition found. In affections occurring during early generalised syphilis the initial dosage of neoarsphenamine may require modification. Rapid symptomatic improvement follows with complete recovery. The ordinary dosage can then be continued. In the late stages it must be remembered that a varying degree of fibrous replacement of the muscular and elastic structure has

already occurred and while it is possible to obtain symptomatic relief it is impossible to reconstitute the normal anatomical structure of the parts. Every effort must however be made to arrest the degenerative process and to secure for the individual the maximum clinical improvement. The general principles are —

(1) *Absolute rest in bed* the administration of digitalis other cardiac drugs according to the ordinary medical principles

(2) The administration of *potassium iodide* in dosage of grs. xxx or grs xl t d.s for a period of two or three weeks.

(3) Administration of *bismuth preparations* commencing with small dosage (0·05 gm. bismuth metal) twice weekly for three to four weeks. The exhibition of iodides should be continued

(4) Administration of *arsphenamines* According to the rapidity of improvement following rest iodides and bismuth arsphenamine administration should be commenced earlier or later Small trial doses (0·075 gm.) may be given twice weekly Intramuscular sulpharsphenamine is preferable to intravenous injection.

(5) If these small doses of bismuth and sulpharsphenamine are well tolerated the strength may gradually be increased to a maximum of 0·2 gm bismuth and 0 3 gm. sulpharsphenamine. The dosage must be adjusted so as to avoid even any slight or transient treatment reactions.

Courses of ten weeks duration should be carried out after which a rest period of from two to four weeks is allowed During this time the exhibition of digitalis should if necessary be continued or pil. Guy i t.d.s. may be substituted Assessment of clinical progress should be made and treatment continued until the maximum clinical improvement is attained. Subsequent treatment should be directed to maintain this improvement

In cases in which it is found that arsenobenzene or *bismuth is not well tolerated, improvement may follow* the substitution of acetylarsan tryparsamide or colloidal mercury sulphide. Penicillin has been employed in the treatment of cardio-vascular syphilis but final assessment of its value is not yet possible.

Blood Changes in Syphilis.—In early generalised syphilis there is usually little change in the erythrocyte count. Anæmia is found more especially in women and the red cells may show a drop of twenty to twenty five per cent In late syphilis extreme anæmia may occur both the red cells and the hæmoglobin showing proportionate reduction. Cases simulating pernicious anæmia have been reported as being due to syphilis and showing rapid improvement under anti-syphilitic therapy A slight or moderate leucocytosis may occur in the secondary or tertiary stages, the differential count being usually within normal limits.

Syphilis of the Spleen.—The spleen may show enlargement in early generalised syphilis The enlargement is *most frequently* firm and painless occasionally the enlarged spleen may be soft and tender on palpation In late syphilis single or multiple large or small gummata may occur Cicatrices result from healing Perisplenitis may give rise to a markedly thickened capsule Amyloid changes may occur especially in association with long untreated hepatic or osseous lesions

Syphilis of the Lymph Glands.—The enlargement of the lymph glands in primary and secondary syphilis has already been described In late syphilis gummous changes may affect a solitary gland or a group of glands. The glands show uniform elastic enlargement but softening leading to sinus formation may occur Periadenitis is not uncommon the resulting clinical picture strongly suggesting tuberculosis.

CHAPTER VIII

MANIFESTATIONS OF SYPHILIS IN OTHER VISCERA, ORGANS, AND GLANDS

THE frequency and importance of syphilitic involvement of the cardio-vascular and nervous systems are widely recognised. Specific disease affecting other viscera organs or glands is however seldom diagnosed. This may be in part due to the fact that syphilis is still considered principally as a disease of skin and bone whereas for at least two decades it has progressively become a more insidious and clinically in apparent internal disease, giving rise in the period of latency to vague symptoms and detectable with certainty only by serological tests. It seems possible on analogy with cardio-vascular and neuro-syphilis that the wider appreciation of possible syphilitic causation would lead to the detection of many more cases of visceral disease due to this cause.

While the student is referred to the larger systematic text books for complete details the m re important changes resulting from syphilitic involvement of other viscera, glands and other tissues are briefly indicated.

Syphilis of the Endocrine Glands.—Involvement of the thyroid the thymus the supra renals and the pituitary may occur in any stage of generalised syphilis while as a result of the vascular changes in congenital syphilis their development may be seriously impaired. It seems not improbable that a number of the signs of congenital syphilis are due to endocrine dysfunction. In general the changes are due (1) to interference with the blood supply leading to faulty development or functioning (2) diffuse

gummous interstitial infiltration leading to cicatrical changes or (3) solitary or multiple gummata. The resulting dysfunction presents no characteristics peculiar to syphilis and the possibility of syphilitic causation must be confirmed by serological and therapeutic tests.

Syphilis of the Respiratory Tract.—Symptoms referable to the *larynx* occur in the stage of early generalisation of syphilis. Mucosal lesions corresponding to diffuse erythematous pharyngitis occur and may be associated with some sub-mucosal œdema. Papules and condylomata have been described as occurring upon the edges of the vocal cords. The prominent symptom is hoarseness or loss of voice. In late generalised syphilis diffuse gummous ulceration solitary gumma leading to ulceration or perichondritis commencing in the arytenoid cartilage may occur Diffuse gummous infiltration gives rise to cicatricial contracture and stenosis. Ulcerating gummata may suggest tuberculous or cancerous lesions. In these pain is a prominent symptom which is absent in gumma. The diagnosis of syphilis depends on the clinical and serological findings and on the effect of treatment Antispecific treatment is followed by rapid improvement

Syphilis of the Bronchi—Bronchial lesions commonly occur in association with tracheal syphilis Catarrhal symptoms occur in the secondary stages while the later manifestations are (1) localised gummata or (2) diffuse gummous infiltration involving any or all the coats of the bronchi and leading to stenosis or bronchiectasis.

Syphilis of the Lungs—Single or multiple gummata of varying size may occur in the fibrous septa near the hilum subsequent caseation giving rise to cavity formation. Interstitial gummous infiltration radiating from the hilum towards the periphery of the lower lobe is more common leading to thick fibrous tissue bands Bronchiectasis may follow cicatricial contracture According to the lesions

present the symptoms may suggest malignant disease or fibroid tuberculosis. The diagnosis depends upon the history clinical findings serological confirmation of syphilis, upon the absence of bacteriological evidence of tuberculosis and upon the result of specific treatment Gummous lesions resolve rapidly interstitial lesions may show little X ray improvement although the patient is symptomatically much benefited.

Syphilis of the Alimentary Tract.—*Stomach*—Alterations of acidity may occur in association with the early generalisation stage of syphilis hypo-acidity not reacting to the usual medical treatment being more common than hyper-acidity In late syphilis ulcerating gummata give rise to tumour-like masses or diffuse gummous infiltration of the walls leads to leather bottle stomach. The serology is positive and specific treatment rapidly effective

Syphilis of the Intestines—Localised gummata or diffuse gummous infiltration with subsequent fibrous tissue formation and liability to cicatricial contracture occur in the colon and rectum. In the latter site the infiltration and stricture formation may lead to the *ano-rectal syphiloma of Fournier*—marked thickening and rigidity of part or whole circumference of the wall of the gut loss of resiliency and irregularity caused by transverse ridges of thickened fibrous tissue Ano-rectal syphiloma must be differentiated from the more common anal stricture of lymphogranuloma inguinale and from malignant disease

Syphilis of the Liver—In early syphilis, jaundice with slight liver enlargement may occur This is due to catarrhal cholangitis to pressure of enlarged lymphatic glands on the portal fissure or to parenchymatous changes. These early manifestations clear up rapidly with anti-syphilitic treatment Acute yellow atrophy may follow parenchymatous hepatitis in the early stages or in tertiary syphilis. Single or multiple gummata are infrequent. Diffuse

gummous infiltration occurs in late syphilis leading to cirrhotic changes. The resulting symptoms may suggest portal cirrhosis tumour (simple, malignant or parasitic) or cholelithiasis. Amyloid changes may follow chronic hepatic syphilis

The *pancreas* may be the seat of localised gumma formation or of diffuse gummous infiltration leading to interstitial fibrosis with glycosuria.

Syphilis of the Genito-Urinary Organs.—In early generalised syphilis transient albuminuria is frequently met with. Rarely acute or subacute nephritis with severe hæmaturia has been recorded, with renal œdema rapidly developing into general anasarca. These symptoms and signs fail to respond to the ordinary methods of treatment but clear up rapidly after the institution of anti-syphilitic treatment In late syphilis, gummata may occur in the kidney or interstitial gummous infiltrations give rise to chronic interstitial and parenchymatous changes with later cirrhotic contraction of the organ.

Similar kidney lesions occur in congenital syphilis In addition paroxysmal hæmoglobinuria may be met with.

Syphilis of the Bladder—In secondary syphilis lesions corresponding to the macular or papular lesions have been described. In tertiary syphilis gummatous lesions may develop insidiously Ulceration of the gumma causes progressively severe hæmorrhage In *tabes* the bladder function may be disturbed early or late in the disease The symptoms are very similar to those observed in prostatic obstruction—difficulty in commencing the act intermittent flow (' stammering micturition) partial or complete retention and overflow incontinence Infection invariably follows retention and is shown by a constant dribbling of foul alkaline hazy urine Examination reveals a varying amount of residual urine without demonstrable mechanical obstruction Cysto-

scopy shows trabeculation of the bladder relaxation of the internal sphincter elevated hypertrophy of the trigone and generalised cystitis. An increased measure of control of micturition and of emptying the bladder follows tryparsamide and fever therapy The cystitis should be treated by the customary measures—lavage with 1/20,000 silver nitrate solution 1/10 000 oxycyanide of mercury or 1/8,000 to 10,000 potassium permanganate. The exhibition of sulphonamides or of mandelic acid is of undoubted value. Local treatment should be con tinued until the infection is cleared ultimate relief of the condition depends on perseverance with systemic treat ment.

The *prostate* may be involved in late generalised syphilis. An interstitial gummous infiltration leads to irregular hard nodular enlargement one lobe being more prominently affected. The symptoms are those of prostatic enlargement the cartilaginous enlargement on examination suggests malignancy Local measures are valueless but there is rapid improvement under antiluetic treatment The diagnosis is retrospective and rests on the rapid improve ment, under treatment in a patient with a positive Wassermann reaction

The *spermatic cord* may be the seat of nodular deposits during the period of the secondary eruption or of gummata during the tertiary stage. Lesions in the cord are com- associated with involvement of the epididymis or testicle.

The *epididymis* may be involved in secondary or ter tiary syphilis. In the former case small nodules commonly tiple and varying in size from a pea to a cherry occur in the upper pole less commonly in the middle or lower Gummata occur as hard indurated nodules in any portion of the epididymis. These conditions have to be differentiated by the therapeutic test from tuberculosis

or malignant disease. The response to anti-syphilitic treatment is prompt The *testicle* is liable to involvement during the tertiary stage of syphilis Localised gummata of varying size may occur in the body of the gland or diffuse interstitial gummous infiltration gives rise to a painless often bilateral swelling On examination the affected organ is strikingly heavy testicular sensation is lost early there is no enlargement of the lymphatics or regional lymph glands. A small hydrocele may be present Syphilitic orchitis must be differentiated from tuberculous disease gonorrhoeal epididymitis hæmatocele neoplasms, and the orchitis associated with mumps. The epididymis is most frequently involved in tuberculosis and gonorrhœa the body of the testis escaping involvement In neoplasm the growth is more rapid than in syphilis and testicular sensation is not lost so early The therapeutic test is most valuable it must be remembered however that the occurrence of a positive Wassermann does not automatically exclude the possibility of malignancy If any doubt remains after a fortnight's treatment with neoarsphenamine bismuth and massive doses of iodides surgical exploration should be carried out without delay The orchitis of mumps is frequently bilateral is much more rapid in onset and is associated with swelling of the parotid and submaxillary glands

The *uterus uterine tubes* and *ovaries* may be the seat of localised interstitial infiltration leading to sclerosis or less commonly of solitary gumma formation

Syphilis of the Eye.—In acquired syphilis iritis is not infrequent during the early or late generalised stage *Iritis* despite its various causation present *certain* common features pericorneal injection due to dilatation of the anterior ciliary vessels giving rise to the characteristic deep pink colour The aqueous is frequently turbid from exudate Adhesions of the iris are common

giving rise to the characteristic irregular pupils. The differentiation from other causes of iritis is by the presence of other signs and symptoms of syphilis positive serology and the response to treatment Single or multiple gummata are rare but may occur in any part of the eye.

Choroiditis may occur either in the early or late stages of generalised syphilis, the patient complaining of dimness and distortion of vision Both eyes are usually affected and ophthalmoscopic examination reveals yellowish or greyish foci of inflammation scattered throughout the fundus a slightly cloudy and oedematous retina and small diffuse opacities in the posterior portion of the vitreous.

Optic atrophy is not infrequent in neuro-syphilis. *Interstitial keratitis* is dealt with under congenital syphilis. Paresis of the ocular muscles is not infrequently an early localising sign in neuro-syphilis

Treatment —The principles applicable to cardio-vascular syphilis also apply to the treatment of syphilis of the other viscera. The sequence of iodides followed after a period of two to three weeks by the cautious administration of bismuth preparations and finally by the exhibition of small doses of arsphenamine, conduces to the arrest of the syphilitic process and the maximum recovery of function of the affected viscus. Reports indicate that improvement may follow penicillin therapy the value of this drug in the treatment of visceral syphilis has not yet been accurately assessed.

CHAPTER IX

NEURO-SYPHILIS

SYPHILIS is one of the most important causes of organic disease of the central nervous system and at any time after the generalisation of the infection there is grave possibility of involvement of the meninges blood vessels or parenchyma of the brain or spinal cord. Symptoms and signs of neuro-syphilis may appear before or concurrently with the appearance of the secondary eruption more commonly however their onset occurs after an interval varying from one to fifteen years or more During this latent period the symptoms may be vague *e g* neurasthenia headaches etc not directly suggestive of neuro-syphilis. Failure to consider this possibility may result in irreparable tissue destruction before the true diagnosis is reached.

Classification of Neuro-syphilis.—According to the predominant localising symptoms and signs neuro-syphilis may be classified —

(1) *Meningeal* —

(*a*) Acute. (*b*) Asymptomatic or with mild symptoms.	Occurs in early or late syphilis. Commonly localised to meninges at base of brain may be diffuse The spinal meninges may be involved alone or in association with basal or diffuse meningitis.
(2) *Vascular*	Early or late in disease

(3) *Parenchymatous* —
   (*a*) General Paralysis
   (*b*) Tabes Dorsalis.
   (*c*) Tabo-paresis.

(4) *Gummata of brain or spinal cord*
(5) *Myelitis*
(6) *Syphilis of the peripheral nerves*

Pathology—The above classification is a useful guide in indicating the structures mainly involved. On the other hand it must be realised that the underlying pathological changes are invariably more diffuse than is suggested by the signs and symptoms and that in many cases more than one group of structures is involved. The pathological basis of neuro-syphilis is similar to that in other tissues an obliterative endarteritis with perivascular small round cell and plasma cell infiltration leading to meningeal thickening, and progressively to impaired nutrition chromatolysis vacuolation, and ultimately complete destruction of the parenchymal cells, with increase of interstitial tissue.

Meningeal Syphilis.—In the majority of cases the basal meninges are involved, but the process may be diffuse. Early or late syphilitic meningeal involvement may be asymptomatic more commonly however headache of varying severity insomnia, slight dizziness, general lassitude, inability to concentrate or perform routine tasks or nervous irritability may be complained of Paralyses are common the third fourth sixth and occasionally the seventh cranial nerves being involved. Monoplegias paraplegias or epileptiform seizures may occur In congenital syphilis, hydrocephalus may result from basal meningitis. Involvement of the spinal meninges gives rise to localised or diffuse motor or sensory symptoms.

Asymptomatic neuro-syphilis should be suspected and

spinal fluid examination made in (1) patients showing a persistently positive Wassermann reaction despite long-continued treatment (2) patients whose blood Wassermann reaction fluctuates from positive to negative despite adequate treatment and (3) patients under treatment for syphilis complaining of persistent headaches or other vague symptoms referable to the central nervous system.

Diagnosis.—Meningeal syphilis has to be diagnosed from functional nervous disorders such as neurasthenia or neurosis and from the early stages of organic disease simulated *e g* disseminated sclerosis. The examination of the spinal fluid is conclusive

Prognosis.—The response to treatment of meningeal syphilis is almost invariably good symptoms are promptly relieved and the cerebro-spinal fluid rapidly becomes normal under treatment with neoarsphenamine or tryparsamide and bismuth

Vascular Neuro-syphilis.—Involvement of the cerebro-spinal blood vessels may occur early or late in the course of generalised syphilis the clinical picture resulting from partial or complete vascular occlusion or from thrombosis or hemorrhage into the brain substance The symptoms are at first mild and transitory becoming progressively more severe. Headache vertigo progressive loss of mental powers and transient paralyses occur Later a definite clinical picture—monoplegia paraplegia or hemiplegia develops often without loss of consciousness or of loss of control of the sphincters. Rupture of a vessel may cause sudden death Aneurysm formation may affect the circle of Willis.

Diagnosis.—The occurrence of cerebro-vascular phenomena in an adult often under the age of forty years, and the absence of evidences of peripheral vascular disease should suggest the possibility of syphilitic causation Generalised cerebral arterio-sclerosis is rare but may

occur at this age. The cerebro-spinal fluid may show no abnormalities. Usually however the cell count is raised the globulin content is increased the Wassermann reaction is positive and the gold-sol reaction shows a luetic curve.

Prognosis.—In partial paresis due to incomplete vascular occlusion, spontaneous recovery may ensue, or the condition clear up rapidly under treatment When hæmorrhage or thrombosis has occurred recovery is more complete than in cases of non-specific causation

General Paralysis of the Insane (*G P.I General Paresis Dementia Paralytica*) —The onset of general paresis may occur from three to fifty years after infection the usual time interval being fifteen to twenty years Males are more commonly affected than females. The initial symptoms are frequently vague and indefinite, the individual being apparently neurasthenic or complaining of headaches insomnia inability to concentrate or absent-mindedness In other cases irritability intemperance, extravagance or deterioration of personal habits may cause the patient s relatives to seek advice. There is difficulty in association and loss of memory for recent events.

The impairment of mental powers is progressive and as the condition advances delusions of grandeur or extreme melancholic depressions develop *Convulsive seizures* may occur the patient becomes unconscious and remains so for periods varying from a few hours to a day or two These convulsions may suggest uræmia or diabetic coma The *speech* becomes thick and slurred, syllables being missed out and the consonants run together Over action of the facial muscles and *tremors* of the lips and tongue are observed during articulation The ***handwriting*** often shows characteristic changes because of muscular tremor familiar words are misspelt or omitted The ***physical*** signs are few and in the earliest stages may not be well

marked. Irregularity of the pupils (the result of previous iritis) a sluggish reaction to light and fine tremor of the muscles of the face tongue and hands may be present. The tendon reflexes are normal or exaggerated. Disturbances of heat and cold sensation may occur affecting especially the legs. Later inequality in size of the pupils loss of pupillary light reaction marked exaggeration, or loss of the tendon reflexes and an extensor plantar reflex may be found. Occasionally some degree of ataxia may be noted.

Diagnosis.—General paresis of the insane has to be differentiated from neurosis chronic alcoholism melancholia neurasthenia intracranial tumours and from generalised cerebral arterio-sclerosis. These conditions may be differentiated on clinical grounds and by the absence of the serological reactions associated with syphilis

Examination of the Cerebro-spinal Fluid.—In the confirmation of diagnosis or exclusion of neuro-syphilis, and in the control of treatment examination of the cerebro-spinal fluid (C.S.F) is of the utmost importance, and should be carried out in all cases showing symptoms or signs suggestive of involvement of the central nervous system. Many authorities advise routine examination of the C S F during the first six months of treatment of generalised syphilis and there is general agreement that all cases of treated syphilis should have a complete C.S.F examination carried out before being discharged as cured. The specimen of cerebro-spinal fluid is usually obtained by a lumbar puncture Cisternal puncture has been advocated but has not come into general use.

Lumbar Puncture.—The specimen of cerebro-spinal fluid is obtained by the introduction of a needle between the 3rd and 4th or 4th and 5th spinous processes of the lumbar vertebræ and entering the lumbar cistern at this

level. No special equipment is needed apart from a lumbar puncture needle of the White-Jeanselme or Dattner pattern. The latter has an outer needle of the same gauge as the White-Jeanselme instrument and a finer inner needle occluded by a stilette. The advantage is that if the theca is punctured by the finer bore needle the spinal fluid may be collected with less risk of subsequent leakage and post-operative headache while accidental puncture by the larger bore needle entails no great risk.

Preparation of the Patient—No special preparation of the patient is necessary The bowels should be moved by



Fig 22
Dattner Spinal Puncture Needle.

a mild saline aperient a light meal should be taken not less than two or three hours before the puncture. In the case of a nervous patient premedication with potassium bromide or morphine may be advisable. Lumbar puncture may be carried out with the patient sitting up or lying on the side according to the individual preference of the operator

The skin over the lumbar spines is washed with ether soap and water dried, and sterilised with tincture of iodine. It is of assistance to delineate the iliac crests with this antiseptic The subsequent stages in the operation are —

(1) Bending the patient forward, by flexing the head and continuing to flex the spine arching out the back and separating as widely as possible the spinous processes of the lumbar vertebræ.

(2) The tip of the spinous process of the 4th lumbar vertebra lies in the horizontal plane joining the highest points of the iliac crest this point is determined.

(3) The interspace between the 3rd and 4th or 4th and 5th lumbar spines is infiltrated with 1 per cent. novocain. An intracutaneous wheal is first made in the mid-line of the body and the needle then directed deeply through the ligaments towards the meninges infiltrating the tissues with anæsthetic. Two to three c.c. may be required

(4) The spinal puncture needle which should have been sterilised by boiling in distilled water and allowed to cool is then picked up by the hilt and held firmly between the thumb and forefinger of the right hand The point is entered horizontally in the centre of the intracutaneous wheal and directed horizontally through the interspinous ligament towards the theca. The needle is gradually inserted until a sudden loss of resistance indicates that the point has penetrated the theca In the event of the needle striking bone it should be partially withdrawn and re-inserted in a slightly different angle according to the position of the lumbar spines. The stilette is now withdrawn and the first few drops of spinal fluid allowed to escape From four to six c.c. of fluid should be collected in a sterile test tube for examination Very slow or intermittent flow may indicate that the needle point has not completely entered the theca or that the eye is obstructed by one of the filaments of the cauda equina This may be remedied by partial rotation of the needle or by inserting it slightly further

After collection of the specimen the needle should be rapidly withdrawn and the site of the puncture mopped with tincture of iodine after which a collodion dressing is applied. The patient should rest in the prone position with the pelvis raised on a pillow or sandbags for at least two hours, and if possible remain in bed without a pillow for the subsequent twelve to twenty four hours. These measures decrease the possibility of post-operative leakage of the C.S F which is the cause of post puncture head

the. Puncture headache may be mild or of extreme verity and is frequently associated with nausea and . It may last only a few hours or may persist seven to ten days. Headache is less common after a puncture with a fine-bore needle and slow collection the fluid The intramuscular administration of 1 c.c. ituitrin immediately after withdrawal of the fluid is of ue in prevention. Established puncture headache sappears when the patient lies down with the head low out recurs on rising In milder cases relief may follow administration of aspirin — phenacetin — caffeine blets, or pyramidon salicylate in doses of gr x, four hourly Impletol* in dosage of 1 to 2 c.c. intramuscularly or ergotamine tartrate frequently controls the symptoms. very severe cases the exhibition of morphia may be uired. If meningismus and pain in the nape of the are marked the local application of a mustard blister is of value. Vomiting is controlled by the hypodermic dministration of atropine sulphate gr 1/100

The incidence of post puncture headache has been greatly diminished by the use of the Dattner needle. The same technique is followed until the outer needle sheath is considered to be near the theca. The inner needle is then freed by releasing the fixing screw and then gradually ding forward until the theca is entered The stilette is ow withdrawn. If no cerebro-spinal fluid escapes the needle is withdrawn and the larger needle introduced little further the inner needle then being advanced as ore until the theca is punctured After collection of the cimen the fine bore needle should be completely withdrawn to make certain that the lumbar cistern has not been penetrated by the larger bore needle after which this, too is withdrawn. After the operation is complete patient should rest in the prone position for twenty

* Bayer

minutes Complications are rare and of much less severity than with the larger needle.

Cisternal Puncture—Puncture of the cisterna magna has not come into universal use because of the apparent danger of damage to the medulla or hæmorrhage from the dural plexus. The cisterna magna lies immediately in front of the occipito-atlantoid ligament Puncture is performed with the patient lying on the side with the neck moderately flexed and the head supported on a firm sandbag so that the cervical spine is horizontal. The hair in the region of the occiput is shaved and the skin over the occipito-cervical area is carefully sterilised with tincture of iodine After novocain infiltration of the skin in the mid line at a point midway between the occipital protuberance and the spine of the axis the needle is introduced and directed along an imaginary line joining the glabella and the mid point of the external auditory meatus. The distance from the skin surface to the occipito-atlantoid ligament is from 3 to 5 cm. Immediately under the ligament are the dura mater and the arachnoid membrane The subarachnoid space is from 1 5 to 2 cm. in depth. The needle must therefore be introduced for a distance of 3 5 to 5 5 cm. before fluid is obtained. A specially marked needle may be employed or an ordinary lumbar puncture needle with marks 5 5 to 6 cm. from the point Headache following cisternal puncture is stated to be much less frequent than after lumbar puncture

During puncture the pressure of the cerebro-spinal fluid should be estimated manometrically Estimates of pressure based on rapidity of flow through the needle are valueless. If lumbar puncture is performed with the patient on the side the pressure of the spinal fluid varies normally from 60 to 150 mm. of cerebro-spinal fluid. In general paralysis of the insane and in many cases of

meningeal reaction the pressure may be markedly increased. Nervousness in the patient any compression over the jugular veins, or interference with free respiration may however result in marked increase of pressure

After collection of the specimen the following observations are made —

(1) Colour and appearance of the fluid.
(2) Cell count.
(3) Increase of protein.
(4) The Wassermann reaction
(5) The gold-sol (Lange) reaction

Normal cerebro-spinal fluid is clear and colourless and has a specific gravity of 1 004 to 1,008 The number of cells varies from 0 to 5 per c.mm. These consist of large and small lymphocytes, with occasionally a large mononuclear cell. A lymphocyte count between 5 and 10 per c.mm. is considered suspicious more than 10 is definitely pathological if the specimen has not been contaminated by blood during the puncture. Globulin is absent or only the faintest trace can be demonstrated.

In neuro-syphilis the macroscopic appearances of the C.S.F are unaltered. In syphilitic meningitis and the early stages of G P.I. *cell counts* of over 250 per c.mm. may be met with. A moderate increase of from 10 to 50 cells " c.mm. is more usual, and is found in all forms of neuro-philis. Small lymphocytes predominate plasma cells " however be present

The *protein* content of the spinal fluid is constantly creased in all types of neuro-syphilis—a very marked ... being common in general paresis and tabes.

The *Wassermann reaction*.—The technique of the Wassermann reaction applied to the spinal fluid is essentially similar to that with blood serum. No inactivation is however required as the spinal fluid contains no free complement A positive C.S F Wassermann reaction is

minutes. Complications are rare and of much less severity than with the larger needle.

Cisternal Puncture.—Puncture of the cisterna magna has not come into universal use because of the apparent danger of damage to the medulla or hæmorrhage from the dural plexus. The cisterna magna lies immediately in front of the occipito-atlantoid ligament. Puncture is performed with the patient lying on the side with the neck moderately flexed and the head supported on a firm sandbag so that the cervical spine is horizontal. The hair in the region of the occiput is shaved and the skin over the occipito-cervical area is carefully sterilised with tincture of iodine. After novocain infiltration of the skin in the mid line at a point midway between the occipital protuberance and the spine of the axis, the needle is introduced and directed along an imaginary line joining *the glabella and the mid point of the external auditory* meatus. The distance from the skin surface to the occipito-atlantoid ligament is from 3 to 5 cm. Immediately under the ligament are the dura mater and the arachnoid membrane. The subarachnoid space is from 1.5 to 2 cm. in depth. The needle must therefore be introduced for a distance of 3.5 to 5.5 cm. before fluid is obtained. A specially marked needle may be employed or an ordinary lumbar puncture needle with marks 5.5 to 6 cm. from the point. Headache following cisternal puncture is stated to be much less frequent than after lumbar puncture.

During puncture the pressure of the cerebro-spinal fluid should be estimated manometrically. Estimates of pressure based on rapidity of flow through the needle are valueless. If lumbar puncture is performed with the patient on the side the pressure of the spinal fluid varies normally from 60 to 150 mm. of cerebro-spinal fluid. In general paralysis of the insane and in many cases of

dilution is added to a test tube containing 5 c.c of colloidal gold solution Alterations of colour are read after the mixture has stood at room temperature overnight the result being expressed numerically or graphically

0 denotes no colour change (ruby red)
1 denotes a very slight alteration to red blue
2 denotes a change to lilac or purple.
3 denotes a change to deep blue.
4 denotes a change to light grey-blue.
5 denotes a complete loss of colour with a heavy blue precipitate.

The characteristic changes in the various types of neuro-syphilis are shown in Fig 103.

It is convenient to summarise here the changes in the cerebro-spinal fluid in the various forms of neuro-syphilis.

Summary of Serological Changes in Various Types of Neuro-syphilis.

	Cells	*Globuli*	*C S F W R*	*Colloidal Gold Reaction*	*Blood W R*
eneral aresis	Increased 0–50 May be 50 or more	Marked increase	Invariably positive	Paretic 5555543 00	Positive
Tabes Dorsalis	Increased 0–50.	Marked increase	Positive	Tabetic or Paretic 34443 00	Positive
leningeal yphilis.	Increased 0–50. May be 50 or more.	Increased	Invariably positive	Luetic 333 0000	Positiv
ascular euro-yphilis	Increased	Increased	Positive	No change or Luetic	Positi

In clinically advanced tabes, and in vascular neuro-syphilis the C S F may show no serological changes

Prognosis.—Confirmation of the diagnosis of general paresis indicates a serious prognosis. If the patient is left untreated there is rapidly progressive mental and physical deterioration leading to death within a few years. Spontaneous remissions which may last for periods varying from a few weeks to several months are not uncommon the patient appearing perfectly normal. The symptoms eventually recur In general the earlier the condition is detected and the less marked the mental and physical changes the better is the outlook. Alterations in speech or advanced mental changes are of grave import.

Treatment.—The application of fever therapy and the introduction of tryparsamide in the treatment of neurosyphilis have materially improved the outlook The neoarsphenamines may temporarily improve the patient's general condition but have no permanent effect on the neural lesions.

Tryparsamide — Tryparsamide is a pentavalent arsenical compound containing 25 per cent of arsenic It is a white odourless crystalline substance readily soluble in water The drug is of low toxicity but before treatment is commenced ophthalmological examination should be carried out to exclude the possibility of optic atrophy When tryparsamide was first issued warnings were given as to the possible danger of optic atrophy following its use this danger has been over-estimated The presence of optic atrophy is considered by some authorities to prohibit the use of this drug others consider that tryparsamide should not necessarily be withheld but that careful observation of the results of cautious administration of the drug should be made In many cases the optic atrophy improves under tryparsamide therapy in others the condition remains unaltered. Progress of the lesion necessitates cessation of tryparsamide In addition to

examination of the fundi, perimetric records of the visual fields should be made contraction of the visual field is the first indication of the toxic effects of tryparsamide.

Examination of the optic discs and perimetry should be repeated at intervals during the course of tryparsamide treatment.

Tryparsamide is administered in dosage of 3·0 gm. weekly concurrently with bismuth in courses of ten weeks duration. A smaller dose should be given at first if there is no untoward reaction this is rapidly increased to the maximum. A rest interval of four weeks is permitted between courses. This sequence should be continued until serological negativity of the cerebro-spinal fluid has been maintained for at least one year

Fever Therapy—Many diverse methods have at one time or another been adopted to produce febrile reactions in the treatment of neuro-syphilis. These fall into three main groups —

(1) Parenteral (or intravenous) injection of bacterial derivatives.

(2) Inoculation of diseases characteristically associated with febrile reaction

(3) Physical.

Bacterial derivatives — The vaccines which are now commonly used are T.A.B Pyrifer * (a *B coli* product) and Dmelcos (p 214) Recently a stock *B coli* vaccine has been employed with satisfactory height and duration of pyrexia and with less marked constitutional symptoms than are frequently associated with T.A.B

Pyrifer or *B coli* vaccine is administered intravenously at two or three-day intervals the progressive dosage being —

* Aristopharm Bâle

N of Injection			3	4	5	6
Dose in millions f Organisms.	5	80–100	50–200	350–400	600–800	1000

No. f Injection	7	8	9			2
Dose millions of Organisms.	400– 600	1000	500	3750	4500	5000–5500

The commencing dose of T A.B should be 25 million organisms.

After each injection the temperature changes should be recorded at intervals of fifteen to thirty minutes the peak of fever is found to vary from 101 to 105 F and the duration from two to six hours. Adequate reactions should be secured by adjustment of the subsequent doses of vaccine. Alternatively in cases in which the temperature curve indicates that a satisfactory degree of fever is not developing a second vaccine injection of approximately half the dosage may be made two or three hours after the first This increases both the height and the duration of the pyrexia.

Inoculation of Disease—A readily inoculable easily curable disease which gives marked intermittent rises of temperature without undue danger to life is essential. Benign tertian malaria (or quartan malaria) fulfils these conditions and is now used to the virtual exclusion of other diseases *e g* rat bite fever or relapsing fever

Malaria therapy using a reliable fever producing strain of plasmodium is applicable to the majority of cases of neuro-syphilis. In elderly and feeble patients its use should be undertaken with caution while patients suffering from concomitant cardio-vascular or visceral lesions must first be treated to secure the maximum physical improvement

Technique of Malaria Inoculation.—Malaria may be induced by mosquito transmission or by the injection of whole blood. The latter method is usually employed as being more certain in effect and less liable to be followed by drug-resistant infection.

Blood is obtained by vein puncture after demonstration of parasites in the peripheral circulation and before the administration of any anti-malarial drugs. The specimen should be citrated, and if immediate inoculation of the patient is not to be practised sealed in a sterile tube which is then packed in a large thermos flask filled with broken ice. The blood remains infective for twenty four hours.

Inoculation should be intravenous (3 to 4 c.c. of malarial blood) if a short incubation period approximately seven days is desired or 5 c.c. subcutaneously in the interscapular region the incubation period being ten to fourteen days. The patient should be hospitalised and confined strictly to bed as soon as the rigors commence Blood films should be examined daily to ascertain the presence and relative numbers of plasmodia. During the febrile periods the temperature should be taken at half hourly intervals Tepid sponging is commenced if the temperature reaches 105 F and discontinued when the temperature has been reduced to 103 F Abundant fluids and large amounts of glucose should be given as a routine digitalis, iron, or other drugs are exhibited according to the indications of the individual case.

Ten to fifteen rigors are permitted before the infection is terminated by the administration of quinine plasmoquin or atebrine

In the majority of cases the course of malaria therapy is uneventful. Mental confusion or delirium and sphincteric incontinence may occur and increase the difficulties of nursing.

N f Injection			3	4	5	6
Dose in millions f Organisms	50	80– 00	50–100	350–400	600–800	1000

No. of Injection	7	8	9		1	
Dose millions of Organisms	400– 600	1000	500	3750	4500	5000–5500

The commencing dose of T.A.B should be 25 million organisms

After each injection the temperature changes should be recorded at intervals of fifteen to thirty minutes the peak of fever is found to vary from 101 to 105 F and the duration from two to six hours Adequate reactions should be secured by adjustment of the subsequent doses of vaccine Alternatively in cases in which the temperature curve indicates that a satisfactory degree of fever is not developing a second vaccine injection of approximately half the dosage may be made two or three hours after the first. This increases both the height and the duration of the pyrexia.

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tive for at least one year Fever therapy may if necessary be repeated after an interval of three to twelve months.

(5) Observation at six-monthly intervals should be con tinued for at least five years, the serology of the blood and C.S.F being tested from time to time during this period

In the event of intolerance to tryparsamide acety larsan or sulpharsphenamine may be substituted. Acetarsol orally bistovol, or tryparson bismuth may be employed in the late stages of treatment.

Penicillin.—Preliminary reports indicate that parenteral penicillin therapy may be followed by clinical ameliora tion of G.P I. and tabes.

A dosage of 10–15 million units is given in fifteen days and this course may be repeated later Intrathecal ad ministration of 20 000 to 50,000 units of penicillin once or twice weekly has been advocated as an additional measure no untoward sequelæ have followed series of from ten to twenty intrathecal treatments. The optimum time dosage of parenteral or intrathecal penicillin therapy and the end results of this treatment have not yet been evaluated until more information is availabl penicillin should not be used alone but should be combined with tryparsamide-bismuth and fever therapy

Paresis-sine-paresi.—In certain cases of untreated syphilis in which the patient presents no mental symp toms of general paresis the spinal fluid is found to give the changes typically characteristic of paresis. It is probabl that in these cases symptomatic paresis would devel p in the course of a few years

Juvenile General Paralysis.—In congenital syphilis children may show symptoms of paresis between the ages of ten and eighteen years Delusions are rar irritability and bad temper are the most prominent arly signs Later occurs The physical signs ar omm nly less marked

a varying or progressive degree of mental impairment children than in adults and many cases therefore escape detection

Tabes Dorsalis (*Locomotor Ataxy*)—The pathology of tabes dorsalis is essentially a posterior root ganglionitis with degeneration of the sensory columns of the lower levels of the spinal cord. It must not be forgotten that there may be concomitant pathological changes in the brain as is shown by the frequency of optic atrophy and cranial nerve pareses.

Symptoms.—The early symptomatology of tabes may show considerable variation. In some cases failing vision, or in others inability to walk, or lightning pains may first call attention to the underlying condition. The cardinal symptoms are —

(1) *Ataxia*—The patient first notices difficulty in walking in the dark or in balancing with the eyes shut when washing the face Later difficulty is experienced in going up or down stairs or over uneven ground The gait becomes characteristic—the feet wide apart raised high thrown forward hyperextending the knee and brought down with a stamping motion *Romberg's sign* is positive—and is an index of muscular hypotonia and incoordination The patient sways and shows a marked tendency to fall when asked to stand with the toes and heels together and the eyes closed.

(2) *Loss of Tendon Reflexes*—The ankle jerk and knee jerk are lost early in the course of tabes The superficial reflexes may also be lost

(3) *Pupillary Changes*—In the early stages the pupils react sluggishly to light later *Argyll Robertson pupils* develop—complete loss of reaction to light reaction to accommodation being present The pupils are frequently small (spinal myosis) are frequently unequal in size and show irregularity in outline

(4) *Ocular Changes*.—*Optic atrophy* progressing to complete loss of vision in three to five years unilateral or bilateral *ptosis* or *paresis of the external ocular* muscles may be the earliest sign

(5) *Lightning Pains* are sharp pains of momentary duration referred commonly to the sciatic distribution Attacks occur at irregular intervals varying from a few hours to several weeks, and become increasingly more severe. Prolonged pains of rheumatic character are not uncommon *Girdle pains* a feeling of painful con striction of the chest or waist and *visceral crises* violent attacks of pain referred to the stomach the larynx the urinary bladder or the kidneys occur and are associated with nausea and vomiting. The temperature is not raised. According to the area involved, appendicitis, renal colic or even gastric perforation may be suggested.

(6) *Sensory Changes* —Areas of *anaesthesia to light touch* occur bilaterally affecting skin areas in the distribution of the 4th and 5th thoracic nerves. *Alterations in pain sense* may affect the legs and be evidenced by delayed conduction, sensation of touch only or loss of localisation of the pain. *Deep sensibility e g* on pressure on bones and tendons is lost

(7) *Sphincters* —Dysfunction of the bladder sphincter is common leading first to delay and difficulty in mic turition, stammering micturition and later retention or overflow incontinence Incomplete emptying of the bladder is frequently followed by cystitis, and ascending urinary infection Cystoscopy reveals a typically trabe culated bladder

(8) *Impotence* —Sexual desire is lost

(9) *Trophic Lesions* —*Perforating ulcers* commonly affecting the ball of the great toe *arthropathies* (Charcot s Joint) *pathological fractures* and *muscular wasting* not infrequently occur

(10) *Mental Powers* show no impairment

Diagnosis.—Tabes must be differentiated from *multiple peripheral neuritis* following alcohol arsenic, diphtheria or diabetes, from *organic diseases* the symptoms of which may be suggested by visceral crises and from *cerebellar lesions* in which ataxia is a prominent feature. The history pupillary signs, and other clinical findings should indicate the possibility of tabes. Confirmation of the diagnosis is made by serological examination of the blood and cerebrospinal fluid *Syphilic meningo-myelitis* may closely simulate tabes the incubation period is however shorter progress is more rapid and recovery under treatment i more rapid and complete

Prognosis.—The course of untreated tabes is unpredictable the condition may progress rapidly to complete paralysis and fatal issue from urinary or other intercurrent infection or may be arrested at any stage. Reactivation and rapid progress may occur after remissions lasting many years

Treatment.—The earlier the diagnosis of tabes dorsalis is made and treatment is instituted the better is the outlook for arrest of the disease Complete recovery never occurs, but stabilisation is possible often with considerable physical improvement Treatment may be considered under the following headings —

General Hygiene —In all cases of neuro-syphilis it is of the utmost importance to secure healthy living conditions for the patient freedom from worry adequate dietary and elimination of any possible foci of sepsis *e g* in the teeth bowels or urinary tract The diet should be plain and nutritious with adequate vitamin content especially Vitamins C and B_1 The bowels should be carefully regulated cystitis if present should be treated by the usual measures. Exposure to cold and wet hould if possible

be avoided the onset of tabetic pains is frequently determined by the approach of wet weather

Specific Treatment—The specific treatment of tabes follows the lines already laid down for general paresis. Chemotherapy with iodides, tryparsamide and bismuth and penicillin should be combined with pyrexial treatment especially in those cases showing marked serological changes in the cerebro-spinal fluid. Treatment should be continued until negative serology has been achieved. In serologically negative cases treatment should be regulated to secure and maintain the maximum of clinical improvement.

Symptomatic Treatment—*Tabetic pains* may temporarily be exacerbated by chemotherapy Relief usually follows the administration of large doses of aspirin phenacetin, and caffeine, or Vitamin B If these fail adrenalin or ephedrine may prove efficacious. Morphia or other drugs of the opium series must be avoided because of possible danger of drug addiction Refractory cases often experience long periods of relief after fever treatment *Visceral crises* may require morphine administration.

Ataxia should be treated by massage and graduated exercises (Frenkel s exercises) designed to re-establish co-ordinated muscular movements. *Urinary incontinence* is generally relieved by routine treatment *Charcot's disease* of a joint should be treated by splinting There is usually little local improvement despite intensive tryparsamide bismuth and fever treatment. In these cases it is wiser to advise a permanent prosthesis, *e g* a walking caliper splint in involvement of the knee joint. Operative arthrodesis is not invariably successful.

Optic atrophy is usually progressive but may be arrested by treatment The possible relationship of tryparsamide therapy to optic atrophy has already been indicated, and

the necessity of examination of the fundus oculi and fields of vision prior to the administration of this drug In cases in which optic atrophy has occurred before treatment has commenced, daily instillations of one drop of 1 per cent. pilocarpine nitrate are of value large doses of iodides should be administered for the first month with concurrent liposoluble bismuth twice weekly At the end of the month tryparsamide should be commenced in small doses cautiously increasing to the maximum The effect of treatment on the optic discs and on the visual fields must be closely observed. In a number of cases further progress of the optic atrophy is arrested When optic atrophy is complete tryparsamide may be administered in the usual dosage from the commencement of treatment.

Cervical Tabes.—Infrequently the pathological changes commence in the cervical segments of the spinal cord the signs and symptoms being referable to the upper limbs.

Juvenile Tabes.—In congenital syphilis tabes dorsalis may occur The onset is frequently insidious and asymptomatic and the condition escapes detection until the disease is far advanced. Argyll Robertson pupils and absence of the knee jerks are the most constant early signs and should always be examined for The onset of optic atrophy urinary disturbances or lightning pains may call attention to the tabes

Tabo-Paresis (*Tabo Paralysis*) —The pathogenesis of tabes and general paresis are essentially similar the anatomical localisation being different Intermediate or combined forms of all degrees may occur *e g* a tabetic onset followed by the mental impairment of dementia paralytica simultaneous progress of tabes and paresis or the "optic-atrophic form of tabes may be followed by paretic mental changes instead of ataxia It is not uncommon to find that the C.S F of a clinically typical

tabes gives serological reactions of G P I Such cases, if untreated later show mental changes.

Gummata of Brain or Spinal Cord.—Gummata are rare but may occur in any portion of the brain. The symptoms are those of brain tumour—optic neuritis headache projectile vomiting, and slow pulse Treatment is rapidly effective Gummata of the spinal cord are usually multiple and are invariably associated with a myelitis

Myelitis.—Syphilitic myelitis is rare Two types occur an *acute transverse myelitis* of rapid onset frequently without preceding motor or sensory irritation. The symptoms depend on the level of the cord at which the lesion occurs. Generally there is complete paralysis from the pelvis downwards with alteration or complete loss of sensation. The temperature sense may remain unimpaired. A *chronic myelitis or meningo-myelitis* is more common and results in an incomplete transverse lesion. The dorsal area is most commonly affected giving rise to vague pains in the back and limbs paraesthesias and motor weakness. Spastic paraplegia may result. Sensory changes are similar to those found in acute myelitis. The tendon reflexes are usually exaggerated and bladder disturbances are common *Erb s syphilitic spinal paralysis* is only one stage in a progressive syphilitic meningo-myelitis

Syphilis of the Peripheral Nerves.—The peripheral nerves may be directly involved, or implicated in syphilitic processes affecting neighbouring structures. Infiltrations of the nerve sheath occur leading to the development of irregular or cone-shaped thickenings, compressing the axis cylinder while vascular changes involving those vessels supplying the nerve lead to impaired nutrition atrophy or necrosis with characteristic sensory or motor changes Gummous lepto-meningitis may involve the anterior or posterior roots of the spinal cord with characteristic sequelae of compression

Neuralgias may occur without apparent anatomical basis. The facial nerve, the intercostals and the branches of the cervical or brachial plexus are most frequently involved. Severe pain is complained of and tender spots occur along the course of the nerve. Specific treatment effects rapid improvement.

CHAPTER X

THE DIAGNOSIS AND TREATMENT OF CONGENITAL SYPHILIS

PRE-NATAL SYPHILIS

IT is now generally accepted that children showing manifestations of syphilis at or shortly after birth have been infected in utero by spirochætes derived from the maternal circulation Congenital syphilis is caused by the same organism as acquired syphilis and the sequelæ of infection are very similar the main differences being that there is no primary sore and that changes may occur from interference with the normal development of the growing organism leading to certain well-marked stigmata. Signs of congenital syphilis do not invariably occur immediately after birth In a number of cases manifestations may be delayed until the age of fifteen to twenty years or even later (*lues tarda*)

Time of Infection of the Fœtus.—Infection of the fœtus is by the transplacental passage of *T pallidum* by the peri-vascular lymphatics of the cord or by an embolus of spirochætes carried by the venous cord blood. Infection seldom occurs earlier than the fifth month of pregnancy

Paternal " transmission " *i.e* infection of the fœtus from infected semen without infection of the mother does not occur In syphilis acquired late in pregnancy—after the eighth month—the infant may escape intra uterine infection but may subsequently develop a typical primary sore after the usual incubation period, inoculation having occurred during the process of birth. Syphilis, acquired in very early infancy may if undetected at the time be later confused with or indistinguishable from congenital syphilis

Course of Syphilis in Pregnancy.—Pregnancy may have little effect on the course of an acquired syphilis the sequence of primary sore skin and mucosal eruptions, etc. occurs at the usual time and presents no marked variation from the same conditions in a non-pregnant woman In many cases however there is a marked tendency to mitigation of the disease the primary sore is trivial and involutes rapidly the secondary manifestations are entirely absent and unaccompanied by constitutional symptoms. The effect of syphilis on child bearing depends on the time of infection syphilis may have been acquired at some time prior to conception at the time of conception or at some later period during pregnancy According to the age of the infection the sequence of early miscarriage still births living syphilitic children and healthy children may result It is assumed that during the course of an untreated syphilis there are recurrent waves of spirochætæmia varying in frequency and duration according to the age of the infection and it is during one of these periods that the fœtus becomes infected. This thesis explains the greater risk of fœtal infection in early syphilis and the later vagaries of transmission of syphilis from an infected mother to her offspring

Syphilis of the Placenta.—The typical syphilitic placenta is larger than normal and its weight ratio to that of the fœtus is one to four as compared with the normal one to six. In appearance it is paler than normal and greasy looking its consistency is softer and sometimes almost friable Infarcts are more numerous. Microscopically characteristic vascular and perivascular changes are seen, the chorionic villi are thicker and more club shaped and the stroma cells are closely packed instead of being stellate An apparently normal placenta may be found in cases in which the fœtus is undoubtedly syphil

Diagnosis of Syphilis in Pregnancy.—The detection of and institution of treatment for syphilis at the earliest moment is of the utmost importance in pregnancy if a healthy child is to be secured. In cases in which clinical signs suggestive of syphilis occur the application of dark ground examination to the exudate from the suspected lesion and the Wassermann reaction will clarify the diagnosis. In the group of cases in which the signs of primary infection are rapidly suppressed and are followed by asymptomatic infectivity the only practical method of diagnosis is by the routine application of serological tests. In these cases the history may be of little help and the physical examination may be entirely negative. The routine application of serological tests is in many cases therefore the only method of determining the presence or absence of a syphilitic infection. Blood Wassermann and flocculation tests should be carried out as soon as pregnancy is certain and repeated at the fourth or fifth and seventh or eighth months. The desirability of repeating the test is judged to a great extent on the history of the individual patient and the possibilities of infection. The specificity and sensitivity of the Wassermann reaction and other serological tests are usually unaltered in pregnancy.

The problem of the false positive Wassermann reaction has already been discussed (p. 31).

Treatment of Syphilis during Pregnancy.—The prevention of congenital syphilis depends on the detection and adequate treatment of maternal syphilis. The pregnant woman tolerates anti-syphilitic treatment as well as the non-pregnant individual and therefore treatment should be as intensive as possible. Penicillin followed by arseno-bismuth therapy should be employed; treatment should be continued from the time of detection of the maternal syphilis up to the time of delivery. If possible it is wise to discontinue the arsenicals two to four weeks before

term to minimise any possible risks of post partum hæmorrhage. A careful watch must be kept for reactions to the anti-syphilitic drugs or for the onset of other complications of pregnancy e g toxæmia In cases in which intolerance to treatment is shown the dosage should be modified to the maximum that is well borne

Any pregnant woman known to have been treated at any previous time for syphilis should receive a full course of treatment during each and every subsequent pregnancy By this means alone can assurance be given of obtaining a healthy child.

The manifestations of congenital syphilis may conveniently be considered as *early* occurring under two years of age and *late* occurring at any later age The manifestations of early congenital syphilis correspond in many respects with those of early acquired syphilis late congenital syphilis although exhibiting many manifestations similar to those of late acquired syphilis shows in addition various stigmata scars or developmental abnormalities resulting from previously active syphilitic lesions. A truly *asymptomatic* infection may also occur no symptoms signs or stigmata being present until the appearance of clinical manifestations Colles s Law—that a syphilitic infant cannot infect its own mother and Profeta s Law—that a mother with manifest syphilis can suckle her own apparently normal infant without infecting it are examples of asymptomatic infection in the mother and child respectively Frank clinical manifestations of congenital syphilis are rare within three or four weeks after birth the earlier clinical signs appear the more serious is the prognosis Late manifestations of congenital syphilis may vary greatly in the time of appearance but not uncommonly occur between the ages of five and seven years at the time of puberty and early adolescence or about the twentieth year

The more important manifestations of congenital syphilis may be tabulated —

Early	Late.	
	Stigmata.	*Active Lesions.*
Fever, wasting, irritability, old-man facies	Rhagades, saddle nose.	Muco-cutaneous eruptions of tertiary type, gummous lesions
	Dish shaped facies	
Muco-cutaneous eruptions	Sabre shins	Periostitis, osteitis.
Snuffles		
Onychia.	Frontal, parietal bossing	Symmetrical hydrarthrosis (Clutton Joints)
Generalised adenitis		
Periostitis, osteitis, osteochondritis	Irregularity of pupils, corneal scars from interstitial keratitis, optic atrophy	Iritis, interstitial keratitis, choroiditis, optic atrophy
Neuro-syphilis, basal meningitis.	Hutchinson incisors, other dental deformities	Neuro-syphilis
Visceral lesions— Liver, spleen, lungs		Cardio-vascular syphilis
		Eighth nerve deafness
		Other lesions as in tertiary acquired syphilis.
Asymptomatic		Asymptomatic
	Detectable only by serological tests	

EARLY CONGENITAL SYPHILIS

General Symptoms.—*Febrile reactions* are not infrequently present in congenital syphilis during the period of the early muco-cutaneous eruption. The temperature is generally irregular, seldom rises above 103 F and falls rapidly to normal after the institution of anti-syphilitic treatment. *Irritability* is not uncommon, sleep is disturbed and there may be fits of severe crying without

obviously adequate cause *Wasting* is frequent but on the other hand undoubtedly syphilitic infants may be strikingly well nourished Marked wasting gives the appearance of great emaciation and marasmus with loss of subcutaneous fat wrinkled *café au lait* skin and a wizened shrunken old man facies.

Cutaneous Manifestations. — Papulo-squamous eruptions corresponding in colour and variation of appearance to those of secondary acquired syphilis are most commonly met with. Macular rashes are seldom seen. The areas most commonly affected are the buttocks and the diaper region the palms and soles and the circum-oral and naso-labial skin. Bullous eruptions infrequently occur (syphilitic pemphigus neonatorum ') on the legs soles of the feet palms and forearms and face.

The main diseases which have to be considered in a *differential diagnosis of these early syphilitic rashes have already been discussed. In addition napkin rashes* and bullous impetigo have to be considered. Napkin rashes may be erythematous vesicular or papular and occur generally on the buttocks back of the thigh calf of the leg and on the heel. Anteriorly they may extend over the lower abdomen to the level of the iliac crests The colour is more erythematous and irritative and there is the characteristic ammoniacal smell. In the papular form the coppery colour and induration of the individual lesions associated with the papular syphilide are missing In the mouth mucous patches must be carefully differentiated from the more commonly occurring thrush

Mucosal Lesions correspond in all respects with those of secondary acquired syphilis The skin rash is frequently accompanied by *snuffles* of varying severity This symptom is due to a secondary mucosal eruption—diffuse erythematous changes mucous patches or moist papules—and may give rise to nutritional disturbances from diffi

culty in suckling At times there is only slight obstruction and snoring nasal breathing (dry snuffles) in other cases there may be profuse purulent or even bloodstained discharge (wet snuffles) Central ulceration of the moist papules leads to involvement of the underlying nasal cartilage or bone with consequent necrosis or interference with later development. This results in the so-called saddle nose. Involvement of the cartilage is often indicated by the peculiar fœtid odour of the nasal discharge. Snuffles or condylomata may be the solitary mucocutaneous manifestation of congenital syphilis. *Laryngitis* occurring at the time of the muco cutaneous eruption gives rise to a suggestive *cracked aphonic cry*



Fig. 104
Vulval and anal moist papules. Note fissuring of anal lesions commencing rhagades.

Rhagades.—The mucocutaneous papules are liable to develop deep fissures in the line of the normal skin folds especially at the angles of the mouth the naso-labial angles or other areas of the upper and lower lip and the chin When the papules heal, linear fissures (rhagades) are left which rarely extend more deeply than the skin These stigmata may also be found at the ano-genital muco-cutaneous junction



Fig 105
Rhagades.

Onychia.—Sub-acute inflammatory changes affect one or more of the nails more commonly those of the fingers leading to opacity and atrophy or exfoliation. Paronychia with free exudation of pus may also occur The **Hair** may show excessive growth in congenital syphilis giving rise to the syphilitic mop or wig Arrest of growth may follow or this may appear insidiously leading to marked generalised or patchy thinning of the hair over the vertex of the skull and the eyebrows **Generalised Adenopathy** *is common in early congenital syphilis* affecting especially the glands of the neck and groin

Periostitis, Osteitis and Osteochondritis —*Periostitis* frequently occurs affecting multiple long bones of the extremities The bone changes may be present at birth or develop later are frequently asymptomatic and are detectable only by routine X ray examination Marked *osteitic changes* are rarely observed in early congenital syphilis *dactylitis* may however occur in the first year of life *Osteochondritis* —Lesions of the epiphyses notably those in relation to the elbow and the knee may be discovered by X ray examination in the early weeks of life long before the occurrence of localising symptoms If the condition is not so diagnosed the history is given that a few weeks after birth (usually within the first three months of life) the use of one or more limbs was lost and that tenderness was a marked feature the child crying on handling of the affected joint (Parrot s pseudo-paralysis) If the arm is affected the paralysis is flaccid while in the leg it is usually spastic There is palpable enlargement and tenderness of the ends of the long bones involved The normal epiphysis is transformed into a thickened irregular wavy opaque yellowish-orange band If the condition is left untreated fatty degeneration or necrosis may lead to epiphyseal separation X-ray examination shows broadening and irregularity of the epiphyseal line

Osteochondritis is distinguished from manifestations of rickets and from infantile scurvy by the earlier age of occurrence the localisation of the syphilitic lesions and the result of the X ray and serological investigations

Cranio-tabes—Thinning of the central area of the occipital



F 06
I ense syphil tic periostit ffec ng humerus, radius and ul (Age 4 months)



Fig 07
S philitic periostitis showing rly sabre-blade t bia (Age 9 months)

and parietal bones may occur in cases of congenital syphilis. The same changes are noted in rickets and it is uncertain whether these changes occur in congenital syphilis unassociated with rickets *Parrot's nodes* consist of thickening of the parietal and frontal bones in the area of the anterior fontanelle and give rise to a somewhat square shaped skull When the bossing is marked the

appearance of four prominences separated by grooves gives rise to the natiform or hot-cross bun skull.

Nervous system and visceral lesions are now seldom met with in early congenital syphilis but should invariably be looked for An insidious or asymptomatic *basal meningitis* may occur leading to *hydrocephalus* which becomes apparent between the third and eleventh months of life Enlargement of the *spleen* and the *liver* from a diffuse interstitial splenitis or hepatitis may be noted at or shortly after birth The degree of splenic enlargement is moderate the margin of the organ seldom extending more than one-half to two inches below the costal margin Splenic enlargement in children under three months of age is highly suggestive but not absolutely diagnostic of congenital syphilis Liver enlargement may be very marked the organ is firm and tender and the lower edge flints on palpation The condition is frequently symptomless jaundice and ascites may however occur early or at some later date from cirrhotic contracture Simple *albuminuria* or *hæmorrhagic parenchymatous nephritis* characterised by generalised œdema marked albuminuria and hæmaturia and a heavy deposit of casts may occur at any time during the first three months of life Paroxysmal hæmo-





FIG 108
Osteochondritis showing thickening and irregularity of epiphyses (also widespread periostitis)

globinuria may occur in later life. The *testes* occasionally show tender firm enlargement which may be followed by atrophy. Eye lesions, *iritis*, *optic neuritis* with atrophy and disseminated choroiditis may be present in the first few months of life. *Pulmonary manifestations* of congenital syphilis are rare in living children. "White pneumonia" is met with in still-born children or in those who survive birth for only a few days. There is fatty degeneration of the alveolar endothelium, the blood vessels show the characteristic vascular and peri-vascular changes and there is marked interstitial fibrosis. It is probable that the lesser degrees of "white pneumonia" compatible with life may be followed in later years by bronchiectasis or chronic fibroid changes.

LATE CONGENITAL SYPHILIS

The late manifestations of congenital syphilis may show great diversity in appearance, varying from almost asymptomatic to gross clinical pictures. The external signs fall into two main groups: (*a*) *stigmata* resulting from previously active syphilitic processes, *e.g.* rhagades, saddle-nose, sabre tibia, corneal scarring from interstitial keratitis, or following interference with normal development, *e.g.* dental anomalies; and (*b*) *actively progressive lesions* often of recent onset. In addition quiescent stigmata, *e.g.* interstitial keratitis, may become reactivated.

The **muco-cutaneous eruptions** of late congenital syphilis are in general strictly comparable to the nodular-cutaneous and gummatous lesions of tertiary acquired syphilis, and need no further description. Not infrequently the eruption may be confined to the circum-oral area, giving rise to a chronic dry scaly "circum-oral eczema."

Bone and Joint Manifestations.—*Periostitis* and *osteitis* may occur at any time during the course of a congenital



Fi 09

Osteitis and chondritis of nasal bon and cartilage late congenital syph lis



I 10

yphilitic osteo-periost t (left lna showing marked ell g (Age 3)



Fio 1

Sabre bl t bia nd Y



I 10

ppear nces

syphilis, but are most frequently noticed between the age of eight and ten years The tibiæ are commonly affected the sclerosing proliferative osteo-periostitis giving rise to the typical sabre-shin of congenital syphilis. The changes may be limited to one part of the bone or involve the whole of the shaft causing a marked increase in girth while deposition of sub-periosteal new bone on the anterior surface most markedly towards the centre of the shaft gives the anterior bowing of the sabre-tibia. This deformity is distinguished from rickets by the increase in thickness of the shaft of the bone and by the new bone formation. In rickets there is no formation of new tissue the curvature being due to a true antero-posterior and medial bending of the distal portion of the bone. *Osteo-myelitis* may occur Infrequently there is associated severe pain suggesting an acute pyogenic infection more commonly however the sub-acuteness of the symptoms and the slowly progressing tissue changes and sinus formation suggest tuberculosis. In syphilis the periosteal and bony thickening extend widely along the shaft of the bone whereas in tuberculosis the periosteal reaction is localised. The serological findings are invariably positive



FIG

X ray syphilitic osteomyelitis with sequestrum formation head of tibia

Syphilis of Joints.—The common joint lesion in congenital syphilis is a painless asymptomatic hydrarthrosis which usually involves one or both knee joints (Clu

Joints) The condition usually develops in early adolescence the onset is insidious and the swelling of the knee is only noticed because of the mechanical interference with full movement of the joint There is no associated muscle wasting The lesion is due to a miliary gummatous synovitis no X-ray changes being detectable in the articular structures Clutton s Joints must be differentiated from tuberculous arthritis by the other evidences of *congenital syphilis* by the absence of confirmatory evidence of tuberculosis by the positive serological reactions and by the rapid effect of treatment The other joint manifestations show little variation from those described under acquired syphilis.



Fig 4
Neglected Clutton J int — commencing osteo-chondro-arthritis

Eye.—Lesions of the eye are not infrequent in congenital syphilis *Iritis* differing in no essential points from that of acquired syphilis may occur at any time after birth. It is commonly bilateral and frequently associated with cyclitis or choroiditis If untreated synechiae may lead to impairment of vision *Interstitial keratitis* is rare in infancy but is common from the eighth to the fifteenth year Later occurrence is, however by no means uncommon. Usually one eye is affected the second eye becoming subsequently involved The onset is slow and insidious commencing with slight ciliary congestion followed by the appearance of faint cloudy or ground glass patches near the centre of the cornea. These gradually spread until the entire cornea becomes lustreless and of dull opacity Vascularisation of the cornea by vessels

derived from the ciliary vessels gives rise to the typical salmon-pink corneal patches.

These changes are associated in the early stages with severe photophobia, supra-orbital pain lachrymation and diminution of vision. If untreated the condition may run its course in a few months leaving an apparently un damaged cornea. More frequently however some opacities or scarring causing impairment of the vision are left. Interstitial keratitis reacts favourably to arsphenamine



FIG. 115.
Interstitial keratitis, showing corneal opacity and down-dra n eyebrow of photophobic habitus.

treatment There is however a great tendency to relapse and it is not uncommon to find an interstitial keratitis affecting the second eye progressing while the first affected eye is improving rapidly under treatment. *Choroiditis* — In the early stages the ophthalmoscope reveals recent foci of inflammatory changes yellowish or greyish spots scattered throughout the fundus. The overlying retina is slightly cloudy and œdematous. Small diffuse opacities are seen in the vitreous usually in the posterior portion. These result from exudate which has passed through the retina. In the later stages organisation of the exudate occurs the resulting fibrosis destroying the normal struc true of the choroid and overlying retina leading to

atrophic spots. Masses of pigment become aggregated round the edge of these atrophic areas The patient complains of diminution of vision If the lesions are situated peripherally vision is little affected while if the macula is involved there is great diminution of vision. Objects appear distorted straight lines appear bent in various *directions infrequently objects appear larger or smaller* than normal. *Optic atrophy* going on to complete blindness may occur at any time in congenital syphilis with or without other localising signs of basal meningitis or neuro-syphilis. The occurrence of optic atrophy should invariably lead to the close examination of the central nervous system.

Ear —In early life a painless suppurative otitis media may follow extension of infection from the nose and throat Eighth nerve deafness occurs from the age of *eight upwards—commonly about puberty—and is frequently* associated with interstitial keratitis. In some cases vertigo and tinnitus precede the occurrence of the nerve lesion. In other cases these symptoms are absent although progressive loss of the upper tone regi ter i occur ring The deafness is bilateral painless and rapidly becomes complete bone and air conduction of sound are equally lost

Hutchinson s Triad.—Interstitial keratitis nerve deaf ness and notched central incisors constitute Hut hinson s triad wh ch is pathognomonic of congenital syphilis

Dental Stigmata.—*Certain dental deformities* occur in congenital syphilis and are of great importance in diagnosis namely *Hutchinson s incisors* and *Moon s molars* The essential factor in the production of these stigmata is the impairment of vascular supply to the developing struc tures This vascular occlusion leads to failure in growth and defective formation of dentine and enamel The classical Hutchinson s incisor is a wedge or barrel-shaped tooth narrower at the incisive edge than at the gum

margin The cutting edge has a central notch Affected teeth may apparently be of normal size, but more commonly show some degree of stunted growth They are spaced more widely than usual and frequently show marked antero-posterior thickening Lesser degrees of the deformity occur and are of value in suggesting the possibility of syphilis the incisive notch may be absent or



FIG. 6.
Hutchinson Incisors (upper and lower central incisors affected)

little marked or the sides of the teeth may be either parallel or show slight or marked convergence towards the cutting edge (screw-driver or peg teeth) The upper permanent central incisors are usually affected symmetrically less frequently one tooth alone shows characteristic changes The lower central incisors are rarely affected. The occurrence of Hutchinson s incisors may be demonstrated before eruption by X ray examination. *Moon s Molars*—The teeth affected are the first permanent molars especially those of the lower jaw Vascular occlusion leads to faulty development of the

tooth giving rise at first to the appearance of a shoulder of enamel bulging out round the crown of the molar From well within the margin spring the four defective dwarfed cusps deficient in enamel These cusps disappear rapidly from caries and attrition giving rise to a dome shaped tooth the coronal surface at first consisting of an irregular mosaic-like pattern and later developing an open honey comb appearance



Fig. 1 7
[Moon Molars, early stage showing defective development cusps

The **typical facies** of late congenital syphilis is a combination of developmental abnormalities and active syphilitic processes or the stigmata following their healing The rhagades corneal haze from interstitial keratitis the flattening of the nasal bridge from osteitis and chondritis Hutchinson s incisors and frontal bossing give rise to an unmistakable picture



Fig 8
Moon Molars, later stage showing dome-shaped tooth th honeycomb coronal surfac

The complete picture is now however seldom met with and instead the general impression conveyed by looking at the face is suggestive rather than pathognomonic A dish-shaped face which is difficult to describe but which is characteristic is commonly met with On analysis the face is found to be concave from forehead to chin and transversely from maxilla to maxilla The causation

appears to be under-development of the pre-maxilla and the maxillæ. In such cases the nasal bridge may show only slight under-development and other stigmata may be present or absent. The expression is frequently apathetic or listless. A photophobic habitus may result from previous interstitial keratitis the head being bent forward and the patient peering from under drawn-down eyebrows.



FIG. 9.
Typical facies of congenital syphilis



F 10
Dish-shaped facies f congenital syphilis

Neuro-syphilis.—It is now recognised that in pre-natal syphilis involvement of the central nervous system is less infrequent than was formerly believed. The symptoms signs and clinical findings may be little marked and the condition progresses insidiously unless detected by careful examination The *basal meningitis* of early congenital syphilis which may be asymptomatic, or associated with irritability convulsions or cranial nerve paralysis, may be followed by hydrocephalus by the later occurrence of epilepsy or by mental deficiency *Cerebral vascular l* as may occur at any time in inf ncy childhood or e ly adolescence. *Parenchymat us neuro-syphilis* usually becomes manifest about the age of puberty but may be

delayed to the age of twenty five or more. In *juvenile paresis* the individual who previously was mentally normal shows progressive *mental deterioration* becoming backward and careless at school or at work. Emotional instability is shown by sudden fits of temper night terrors, perverse roughness or the development of an unruly wildness or outright delinquency Epileptiform fits may be an early sign The delusions and mental exaltation met with in the general paralysis of acquired syphilis seldom occur

The later progress of juvenile paralysis shows little variation from that occurring in acquired syphilis. Involvement of the central nervous system should invariably be thought of in any child suffering from congenital syphilis who shows an increase of nervous irritability conduct disorder or recent mental backwardness Similar symptoms occurring in a child should lead to the con*sideration of the possibility of pre-natal syphilis.* The examination of the spinal fluid and treatment with tryparsamide and fever are as described in adult neurosyphilis. *Juvenile tabes* is frequently asymptomatic and can be detected only by careful routine examination Optic atrophy is frequently associated with juvenile tabes but may occur as an isolated manifestation

The Endocrine Glands.—*All the endocrine glands may* be directly affected by the spirochaete or by vascular occlusion the resulting failure to attain full development accounting for at least some of the dystrophies of congenital syphilis. In some cases syphilis seems to impart a developmental stimulus which expresses itself in hypertrophies of structure and over-activity of which the mental precocity and physique of well-developed syphilitic children are examples.

The Diagnosis of Congenital Syphilis.—The clinical picture of congenital syphilis shows as much diversity as that of acquired syphilis in addition as the chronological

order of the appearance of manifestations (the comparatively sharp division between the secondary and tertiary lesions) is lost puzzling pictures may occur at any time after birth from the admixture of secondary lesions and gummata. In general there is a tendency for the lesions during the first two years of life to be confined to the skin and mucous membranes and to conform more to those of the secondary stage of acquired syphilis. As has been emphasised, however bone and joint visceral, eye and nervous system lesions may be present and can only be detected by the appropriate examination. After the second year of life the manifestations correspond in general with those of tertiary acquired syphilis. In cases showing widespread frank lesions the probability of congenital syphilis should be obvious and should be confirmed by the demonstration of *T pallidum* in the lesions and by serological tests when the lesions are scanty or absent or when there are only vague general symptoms without external signs the possibility of syphilis may be overlooked. Certain additional principles of diagnosis applicable to congenital syphilis may be summarised —

(1) *Clinical signs and serological examination of the individual patient*—In the child it is of the utmost importance that a complete clinical examination should be undertaken. The whole skin surfaces, the accessible mucocutaneous junctions and mucous surfaces should be carefully inspected. Thoracic and abdominal examination should be made to detect any physical abnormalities, especially hepatic and splenic enlargement. The long bones the eyes and the central nervous system must also be examined.

Clinical examination should be supplemented by serological examination and according to the age at which the patient is seen by other special investigations,

If congenital syphilis is suspected immediately after birth microscopic examination of the placenta should be carried out and dark-ground examination of scrapings of the umbilical vein made in the attempt to demonstrate *T pallidum* The umbilical vein is first washed clear of blood and dark-ground preparations are then made from scrapings obtained from the inner wall. Demonstration of *T pallidum* is conclusive proof of infection of the foetus. If it is desired to send material to a laboratory for this examination a specimen of three to four inches of the umbilical cord is sufficient

X-ray examination of the long bones should be carried out between the 10th and 14th day of life. The demonstration of periostitis affecting multiple long bones or the epiphyseal changes of osteochondritis confirm the diagnosis.

The Wassermann reaction or other serological tests may be applied to the cord blood or the venous blood of the infant. The results from the former method are to a great extent invalidated by the high proportion of anti-complementary or false positive results obtained The venous blood Wassermann reaction may give rise to difficulties in interpretation. The test may be negative in undoubted congenital syphilis during the first 10 or 14 days after birth later becoming positive Conversely the transfer of Wassermann reacting bodies from the maternal circulation *e g* from a mother adequately treated but whose serological reactions still remain persistently positive may give rise to a false positive reaction in the infant In such cases there is no clinical evidence of syphilis the child is well nourished X ray examination is negative and without treatment the serological reaction becomes negative in the course of 4 to 8 weeks. Quantitive reactions show a diminishing titre

(2) *Investigation of mother and other members of the family* —The suspicion of possible congenital syphilis in a

child should lead to the examination of the mother and other members of the family A detailed history with special reference to the obstetric record of the mother should be supplemented by complete clinical and serological investigation.

The diagnosis of the late manifestations of congenital syphilis is on general principles the clinical signs, serological findings and evidences of syphilitic infection in other members of the family all having to be taken into account. X-ray examination of the long bones, unerupted incisor teeth or cardio-vascular system may yield valuable confirmatory evidence.

TREATMENT OF CONGENITAL SYPHILIS

The treatment of congenital syphilis should be commenced as soon as the diagnosis is reached. The drugs employed, unit courses and precautions to be observed do not differ materially from those in acquired syphilis The intravenous route is however generally impractic able in younger children and sulpharsphenamine intra muscularly is substituted for neoarsphenamine intra venously In older children with good veins intravenous medication is advisable The dosage of drugs depends on the age, weight and general condition of the child. There are no absolute contra indications to arseno-therapy the initial dose may however have to be greatly reduced in the case of the new born syphilitic infant with marasmus or gross visceral lesions. Improvement is rapid.

Intolerance to therapy is rare in the infant, but it is also frequently difficult to detect the best guide is the clinical progress made and progressive gain in weight

The dosage of neoarsphenamine or sulpharsphenamine should not exceed ·01 gm per kilogram body weight the dosage of bismuth is from one-half to three-quarter of

this amount. The administration of the drugs should commence with one-quarter to one-half of the calculated dose according to the general condition of the patient and should be gradually increased to the maximum. Twice-weekly injections of smaller doses are often to be preferred

A guide to the dosage for various ages is —

	Sulpharsphenamine (gm.) or *Neoarsphenamine*	*Bismuth* (gm.)
Birth to 3 months	·005–·075	5 5
3 to 1 months	·075–	05
to 3 years	1– 5	05 075
8 to 4 years	5–3	5

A course of treatment suitable for a newly-born infant weighing seven to nine pounds can be mapped out —

	Sulpharsphenamine (gm.)	*Bismuth* (gm.)
1st day	·005	
4th day	005	·0 5
8th day	005	
th day	005	5
5th day	005	
8th day	005	5
5th day		5
32nd day	02	5
30th day	02 3	5
46th day	·0 3	05
53rd day	·03– 3	5
60th day	5 5	5

A rest of two weeks is permitted after completion of the first course during which time syrup *ferri iodidi* may be given in dosage of 20 to 30 minims t.d.s. after which the serological tests are repeated. Subsequent courses of treatment and rest periods are mapped out according to the clinical progress the increase in weight and the serological findings. Treatment must of necessity be more prolonged than in the adult a minimum of two years active treatment being essential even for those cases in

which the Wassermann reaction becomes negative soon after the institution of treatment Many cases with persistently positive serology require treatment over still longer periods in these cases active treatment with neoarsphenamines and bismuth should be continued for at least four years before any long rests are permitted. In these cases it is often wiser to continue treatment with moderate dosage in the attempt to secure for the patient permanent freedom from relapse than to attempt to attain negative serology by heroic dosage. The therapeutic effect of different preparations *e.g.* acetylarsan, mapharsen stovarsol may be tried After the end of four years active treatment long rests should be permitted, the child remaining under periodic observation. Many clinicians recommend that one unit course of arseno-bismuth or bismuth therapy should be administered yearly for at least a further four years. During the period of observation the same attention should be paid to the cardio-vascular and nervous systems as in acquired syphilis.

While evidences of intolerance are rare in the infant or child cases occur in which the use of sulpharsphenamine is followed by untoward effects. In these cases acetylarsan may be substituted.

Acetarsone (stovarsol, orarsan) may be administered orally if for any reason parenteral therapy is impracticable The dosage for a new born infant is —

	Acetarsone
1st week	mgm per kilo body weight, daily
2nd week	8 mgm
3rd to 9th week	24 mgm

The tablets should be crushed and given in divided doses in milk or water before meals. After the course has been completed, a rest interval of four weeks is permitted. The blood serology is investigated at the end of the inter-

mission, and subsequent courses of increased dosage according to the body weight of the child continued until a negative serology in the blood and cerebro-spinal fluid has been maintained for one year

The treatment of congenital syphilis at later periods in life is carried out on lines comparable to those in adult acquired syphilis the sole modifications being the employment of doses suitable to the age weight and condition of the patient and the necessary protraction of treatment in sero-resistant cases.

Penicillin.—The effect of penicillin therapy in early congenital syphilis is comparable to its action in early acquired infections causing rapid healing of the muco-cutaneous and osseous lesions and diminution of the Wassermann titre Children have been found to tolerate remarkably large dosages and for infants treated shortly after birth a total of 2,400 000 Oxford units of penicillin ha been given in fifteen days in recent cases totals of 4 500 000 units have been exhibited in the same time period without untoward incident Saline solutions of the drug and three-hourly administration should be employed A careful watch must be kept for the first forty-eight hours to detect any Herxheimer and temperature reactions which necessitate temporary reduction of dosage or withdrawal of the drug

During the period of penicillin administration failure to gain weight or even a slight loss in weight has been noted in the majority of cases this is rapidly made up after completion of the course of penicillin

In the late manifestation ... ital syphili peni-cillin therapy has been f ... by rapid ... of gummatous lesions in ... litions, ... ter stitial keratitis marked ... nt is ... per cent. of the cases.

During the of ... nr ...

two injections of an arsenical should be given and subsequently arseno-bismuth chemotherapy is continued the number of unit courses required in any case depending on the clinical and serological results obtained. Further courses of penicillin may be considered.

CHAPTER XI

CHANCROID

CHANCROID (*Soft Chancre Soft Sore*) is a localised painful genital ulceration due to *Ducrey's bacillus* subject to local complications lymphangitis bubo and phagedena but never followed by constitutional sequelæ. **Infection** is generally by sexual contact Extra genital chancroids rarely occur contagion from infected linen and auto-inoculation *e g* of the fingers from the genital lesions are however possible

Sexual Incidence.—Males especially among the poorer classes and seamen are more frequently affected than females. Examination of the alleged sources of infection may reveal no recognisable chancroidal lesions in the female suggesting the possibility of carrierism or asymptomatic infectivity

The **common sites** of infection are —

Males	Females
Coronal sulcus	Vulva perineum
Frenum	Labia majora and minor
Preputial meatus	*Urethra*
Urethral meatus	Thighs
Glans penis	May occur in vagina and on cervix

Clinical Course.—Following an incubation period of 1 to 5 days the lesions commence either as small abrasions which rapidly break down forming ulcers or as a small inflamed furuncle-like lesion rapidly going on to vesicle or pustule and finally ulcer formation multiple sores occurring from auto-inoculation The resulting sores may

be circular or ovoid but are more frequently irregular with ragged thin red undermined edges and a soft irregular base covered with yellow purulent discharge. A narrow bright red inflammatory areola corresponding to the



Fig 1
Multiple chancroidal ulcers on coronal sulcus and inner aspect of prepuce



Fig.
Chancroidal ulceration of preputial meatus, showing typical fuzzy appearance



Fig 3
Chancroid of corona glandis and fluctuating bubo



Fig 4
Groin ulceration following rupture of bubo

extent of undermining of the edge may be present induration of the sore which bleeds freely on handling or l using i however invariably absent Spread is by erosion of the margins of the sores which starting with a d meter f r t 3 mm may attain a diameter of over an

inch. Superadded pyogenic infection largely determines the extent and rapidity of spread of the ulcer and the



F 1 5
Chancroid of ter aspect f 5th finger
(infection from genital chancroid)



Fig. 126
U thral fistula follow g hancroidal
ulceration f frenal are

resulting tissue destruction this is more marked when the sores are *concealed under a tight prepuce* Pain of a greater or lesser degree i a marked feature

Ulcerated papular forms may occur while occasionally

there is a miliary distribution of minute chancroids over the glans penis and inner aspect of the prepuce.

Complications and Sequelae.—*Painful lymphangitis* is common, and in the male frequently gives rise to in



FIG. 7
Early phagedena affecting glans penis—note blackening of tissue and line of demarcation.



FIG. 8
Phagedena involving integument of penis—line of demarcation immediately distal to pubes.

flammatory phimosis. Early painful *regional adenitis* is the rule. In the absence of treatment suppuration (bubo formation) involvement of the overlying skin and intractable ulceration may follow. This sequence has been noted up to several months after the spontaneous healing of a chancroid. *Hæmorrhage* may occur

from erosion into an artery either during the active progress of the chancroid or in the healing stages the commonest site is from the frenal artery *Fistula* may occur from erosion into the urethra. *Phagedena* (Phagedenic Gangrene) is an acute rapidly spreading gangrene



Fig 29.
Reenstierna intra-dermal test

most commonly associated with chancroid but which may complicate a non-specific ulceration or a primary sore and is most commonly met with in males Predisposing factors are general debility in the patient and the occurrence of sores under a phimotic prepuce Phagedena is always associated with secondary infection and the

presence of Vincent's spirilla and fusiform bacilli. The earliest warning of impending phagedena is in the alteration of the subpreputial discharge which becomes brownish, frequently frothy and emits a characteristic sickly foul smell. The sores show a blackening round the edge with foul-smelling black necrotic sloughs covering the base. Inflammatory œdema of the prepuce rapidly develops and the swollen organ assumes a dusky red or plum colour Tenderness of the part is exquisite. Tissue destruction is rapid perforation of the prepuce may occur in 24 to 48 hours and the necrosis may lead to urethral fistula or extend along the shaft of the penis. *Stricture e g* of the urethra or of the cervical canal may follow the healing of the chancroids in these areas.

Diagnosis.—The clinical diagnosis of chancroid is suggested by the short incubation period and by the characteristics of the sore which contrast sharply with those of a primary chancre. Dual infection with syphilis and chancroid is not infrequent and in every case of suspected chancroid the possibility of concomitant syphilis must be excluded by repeated dark-ground examination and subsequent Wassermann surveillance. Chancroid may be closely simulated by non-specific pyogenic genital ulceration infected traumatic ulceration *e g* at the site of a torn frenum or by a secondarily infected primary sore and must be differentiated from lymphogranuloma inguinale and granuloma venereum

Confirmation of the clinical diagnosis of chancroid rests on the demonstration in smears or by culture of *B ducreyi* from the deeper tissues at the edge of the sore or from the bubo or by the *Reenstierna test* Ducrey's bacilli are seen as minute oval gram-negative rods, approximately 1 5μ long by 0·5μ broad arranged generally extracellularly in small groups or in chains of varying length Demonstration of *B ducreyi* may be rendered

difficult or even impossible by superadded pyogenic infection. The Reenstierna test consists in the intracutaneous injection of 0·2 c.c. of a suspension of killed streptobacilli of Ducrey (Dmelcos Diagnostic) A positive reaction indicating that the patient has, or has previously suffered from a chancroidal infection is shown by the occurrence within 24 to 48 hours of a wheal surrounded by a red halo Infrequently a vesicle may occur at the centre of the wheal this may be followed by central necrosis The intradermal test becomes positive about the eighth day of chancroidal ulceration and may persist for years.

Treatment.—Chancroidal ulceration in general heals rapidly under sulphonamide administration and in the majority of cases no local treatment apart from measures of cleanliness and mildly antiseptic applications is required. A dosage of sulphapyridine sulphathiazole or sulphadiazine of 5 grm. daily for five days is generally adequate but if necessary a further course may be given later The sulphonamides have no effect on *T pallidum* and by controlling chancroidal infection may facilitate its demonstration. During the first three to five days dark ground examinations should be made provisionally to exclude syphilis. During this period the sores are cleansed with saline and powdered sulphur is thoroughly rubbed in with the tip of the finger or a pledget of gauze special care being taken to deal with any undercut recesses at the edge of the sores Later 1 per cent mercurochrome ointment prontosil ointment or sulphapyridine powder may be applied In some cases although extension of infection is controlled a granulomatous ulcer persists which shows little tendency to heal. In such cases cauterisation with thymol iodide 10 per cent in ether pure carbolic acid or the electric cautery may be successful. If the situation of the chronic ulceration *e g* on the

prepuce, permits of excision, this is the method of choice.

When *inflammatory phimosis* renders access to the underlying chancroids difficult massive subpreputial lavage with hypertonic saline at 105 F through a fine cannula twice or thrice daily and application of foments may cause resolution. Persistence of symptoms and signs haemorrhage or the onset of phagedena necessitates exposure of the sores by *dorsal* or *lateral* slitting, by *V-excision* of the dorsum of the prepuce or by *complete circumcision* under gas and oxygen pentothal, or local anaesthesia.

Technique of Dorsal Slit.—If local anaesthesia is chosen, a broad band of infiltration of 1 per cent novocain-adrenalin solution is commenced by making an intra cutaneous wheal in the mid-line of the dorsum of the penis ½ to 1 inch proximal to the coronal sulcus and continuing by subcutaneous injection distally along the line of the projected incision to the preputial meatus. It is essential to use a fine needle to infiltrate the complete thickness of the prepuce, and to allow at least five minutes for the anaesthetic to take effect. Two pairs of Lane's tissue forceps are then applied to the anaesthetised tip of the prepuce one on either side of the mid-line dorsally gentle traction is made and a grooved blunt-pointed director introduced through the preputial orifice and directed between the glans and the inner aspect of the dorsum of the prepuce until the tip reaches the coronal sulcus. Using the groove of the director as a guide and the Lane's forceps to steady the organ the dorsum of the prepuce is now slit with the scissors or a scalpel in the mid line as far back as the coronal sulcus. Haemorrhage is usually slight but ligature of a few bleeding points may be required In general, no sutures are neces ary Ever ion of the preputial flaps permits of compl te inspecti

of the glans penis the coronal sulcus and the frenum and access for treatment of any ulcerated area. The main objection to simple dorsal slit is the ugly ventral preputial flap left on healing which may be remedied by subsequent trimming A better cosmetic end result is by wide V excision of the dorsum of the prepuce If local anæsthesia is used *the entire prepuce should be infiltrated. A dorsal* slit is completed and the preputial flaps are everted. Injection of novocain is now made under the mucosa in the coronal sulcus and towards the base of the glans. The needle is introduced in the dorsal mid line and advanced slowly submucosally in the direction of the frenum each side being in turn infiltrated.

A silkworm or catgut suture is now placed *in the mid* line to approximate the mucosa of the coronal sulcus and the skin edge at the proximal end of the dorsal slit With this point as apex and cutting with curved scissors towards the free border triangular portions of tissue of the desired size are removed from the redundant preputial flaps. Any bleeding points are ligated and one or two apposition sutures are inserted *on either side The wider the* V excision *i e* the closer the lines of the V are carried towards the base of the frenum the more nearly it approaches complete circumcision which is best decided on and completed after performing a dorsal slit and inspecting and treating the underlying lesions. *Lateral Slits* are carried out by local infiltration of the proposed *lines of incision and give excellent exposure of the glans* and coronal sulcus. Subsequent cosmetic trimming is required. Chancroidal infection of the incision rarely occurs now and in general it is wiser except in cases of phagedena to do a complete circumcision Subsequent dressings are by flavine 1 per cent in paraff. liq compound tincture of benzoin or sulphonamide powder *Phagedena* necessitates surgical exposure of the lesion

complete removal of all necrotic tissue and thorough application of the electric cautery diathermic fulguration or acid nitrate of mercury Immediate relief of pain follows and healing is uneventful. In cases in which there has been spread along the penile lymphatics towards the abdominal wall, multiple incisions should be made to provide free drainage, followed by continuous mildly antiseptic baths or applications, *e g* eusol, 1 10 000 solution of potassium permanganate or magnesium sulphate in glycerine. The sulphonamides are of value and should be exhibited in maximum dosage.

Bubo.—The painful regional lymphadenitis and periadenitis associated with chancroid clears up rapidly under sulphonamide administration which may also abort early suppuration. Where, however there is large abscess formation and the overlying skin has become adherent to the underlying tissues and shows a dusky red discoloration aspiration and antiseptic injection are indicated. After sterilisation of the skin a stout gauge hypodermic needle mounted on a 10 to 20 c.c. record syringe is introduced through intact skin at least ½ an inch beyond the area of discoloration, directed subcutaneously towards and finally entering the abscess cavity Aspiration of the pus is followed by washing out the abscess cavity by repeated injection and reaspiration of 2 to 4 per cent mercurochrome solution, colloid iodine or 1/20 dilution of tincture of iodine in distilled water This procedure which may require daily repetition for several days, should be employed in preference to open incision even in those cases where the skin is threatening to break down. Healing is more rapid than with surgical incision and drainage When rupture of the bubo has taken place free incision and curettage of the cavity with a Volkmann's spoon are indicated followed by application of tincture of iodine thymol iodide in ether 4 per cent

mercurochrome or 1 per cent picric acid in spirit Subsequent dressings are by fomentations magnesium sulphate in glycerine and after subsidence of the acute inflammation by prontosil ointment sulphapyridine powder 1 to 4 per cent. mercurochrome ointment or red lotion. *Dmelcos a B ducrey* vaccine given intravenously causes a temperature reaction and is of value in suppurating chancroidal bubo and in the treatment of uncomplicated chancroid The commencing dose of 1·0 c c. (225 million organisms) is increased by ½ c c. every second or third day until a maximum dose of 3·0 c.c. is reached. The temperature may reach 104 to 105 F There is no contra indication to concomitant treatment with Dmelcos and sulphonamides.

Penicillin has proved valueless in the treatment of chancroid and its complications.

Subsequent *Wassermann surveillance* should be carried out for *three months* to exclude the possibility of concomitant syphilis. The tests are taken weekly during the first month and fortnightly during the second and third months.

CHAPTER XII

GONORRHŒA IN THE MALE

ANATOMY OF MALE GENITO-URINARY TRACT

GONORRHŒA is a specific disease caused by a pathogenic micro-organism the gonococcus a Gram-negative diplococcus of the Neisserian group the primary site of infection being the mucous membrane of the genito-urinary tract of the male or female. Direct local extensions of infection involve other genito-urinary structures while blood-stream infection results in meta static complications of which arthritis is the most common.

Modes of Infection.—In the vast majority of cases genital infection with the gonococcus follows sexual inter course with an infected person. Undoubted cases of accidental contagion of the male urethra are excessively rare asexual infection of the adult female, for example from lavatory seats or infected towels, is theoretically possible The vast majority of cases of accidental infec tion however are those of vulvo-vaginitis in girls before puberty and the rare cases of sporadic gonococcal ophthalmia *i.e* purulent gonococcal conjunctivitis with-out concomitant genital infection.

A knowledge of the anatomy and histology of the genito-urinary tract in both sexes is essential if the possi-bilities of gonococcal infection are to be fully appreciated, accurate assessment of the anatomical extent of infection made and residual foci of infection eliminated.

Anatomical Consideration of Male Lower Genito-Urinary Tract.—The urethra in the male is a channel varying in length from eight to nine inches extending from the neck of the bladder to the urinary meatus,

Anatomically it is divided into three parts (1) the pars prostatica or prostatic urethra *passing through the substance of the prostate gland* (2) the pars membranacea or membranous urethra lying between the two layers of the triangular ligament and (3) the pars cavernosa or penile urethra traversing the entire length of the corpus cavernosum urethræ. The curved, rather ꞷ shaped course of the urethra from the bladder to the external meatus and the fact that it is only a potential canal the walls normally being in contact except during the act of micturition constitute a difficulty to the free drainage of inflammatory products.

For clinical purposes *the* male urethra is divided into anterior and posterior *regions* the anterior urethra corresponding to the penile urethra and the posterior urethra including the membranous and prostatic parts.

The Posterior Urethra and Associated Structures.—The *prostatic urethra commences at the internal urethral* orifice of the bladder and pursues a nearly vertical course of about one and a quarter inches in length downwards through the substance of the prostate to become continuous with the membranous urethra at the posterior fascial layer of the urogenital diaphragm (triangular ligament) The mucous membrane consists proximally of transitional epithelium continuous with that of the bladder and distally of columnar epithelium continuous with that of the membranous urethra This columnar epithelium is continuous also with the columnar epithelial lining membrane of the prostatic ducts and glands and of the common ejaculatory ducts. The proximal three-quarters of an inch of the mucous membrane of the posterior wall or floor is raised to form a narrow prominent ridge called the crista urethræ or verumontanum Upon this ridge is a prominent eminence the colliculus seminalis, on the summit of which is a slit-like opening leading upwards

FIG. 3
Anatomical diagram of male genito-urinary tract

and backwards for approximately one-quarter of an inch, forming a blind pouch the utriculus prostaticus or sinus pocularis. On either side of the prostatic utricle is the minute opening of the common ejaculatory duct while lateral to the base of the crista urethræ are found two longitudinal depressions the prostatic sinuses into which open the prostatic ducts. Immediately under the mucous membrane lies the submucous supporting tissue through which pass the vessels and nerves supplying this area.

The **Prostate Gland.**—This gland surrounds the first portion of the urethra and lies in close contact with the base of the bladder It is firm in consistence and in shape and colour resembles a chestnut. It is normally subject to much variation in size the transverse diameter at the base approximating to one and a half inches, the vertical diameter from base to apex about one and a quarter inches and the antero-posterior diameter about three-quarters of an inch The apex of its conical form points downwards and rests on the posterior fascial layer of the triangular ligament The base directed upwards is in close contact with the base of the bladder

Its posterior surface lies against the anterior aspect of the rectum from which it is separated by a loose cellular and fascial layer The anterior aspect projects between the anterior borders of the levatores ani muscles The gland is composed of three lobes, two lateral lobes separated posteriorly by a vertical median groove and a middle lobe including that part of the basal portion of the gland lying between and above the common ejaculatory ducts

Structure—The prostate is encased in a thin external fibrous capsule derived from the recto-vesical layer of pelvic fascia and an inner fibrous stratum immediately related to the gland substance. Between the two fascial sheaths lies the prostatic venous plexus stretching over the antero-lateral aspect of the gland The substance of

the prostate comprises two elements muscular and glandular The former is of the plain variety and is arranged as a partly longitudinal and partly transverse peripheral layer and an internal circular layer surrounding the prostatic urethra and continuous above with the fibres of the vesical sphincter and below with those of the compressor urethræ muscle surrounding the membranous urethra. Between these two layers the muscular fibres form a reticulum containing the glandular elements. The prostatic glands consist of branched tubular alveoli or acini lined with columnar epithelium These alveoli lead into similarly lined excretory or prostatic ducts which open by individual orifices into the prostatic sinuses

The blood supply of the prostate and prostatic urethra is derived from the inferior vesical, the middle hæmorrhoidal, and the intrapelvic portion of the sciatic vessels The veins from the prostatic plexus join with the vesical veins and pass to the internal iliac vein. Lymphatic drainage from the prostate is to the external iliac internal iliac sacral, and common iliac glands. Innervation is from the pelvic sympathetic plexus.

The prostate secretes a thin opalescent alkaline fluid containing lipoid material, corpora amylacea and various cellular elements.

The **Seminal Vesicles.**—These are two in number lying to the right and left of the mid-line immediately above the prostate and between the base of the bladder and the rectum. They are conical, sacculated reservoirs approximately two inches long and one-half inch broad at the widest part The open medial end of the vesicle is continuous with the narrow seminal duct which joins the corresponding vas deferens at an acute angle to form the common ejaculatory ducts. From the medial aspect the vesicle runs upwards and outwards terminating in the closed broad free end

Each vesicle consists of a highly convoluted tube comprising an outer longitudinal and an inner circular muscular layer lined with non-ciliated columnar epithelium. The coils are bound together by dense areolar tissue diverticula are numerous. The vesicle is surrounded by a fascial sheath derived from the rectovesical layer of the visceral portion of the pelvic fascia. The arterial supply is derived from the inferior vesical the middle hæmorrhoidal, the descending branch of the artery to the vas deferens and the intra-pelvic portion of the sciatic vessels. The large plexiform veins communicate with the prostato-vesical plexus. Lymphatic drainage is to the internal iliac glands innervation is from the pelvic plexus.

The vesicles produce a viscid greyish alkaline secretion which forms part of the seminal fluid

The **Seminal Ducts** and **Common Ejaculatory Ducts** are muscular tubes lined with non-ciliated columnar epithelium. The latter are formed by the junction of the short seminal duct and the vas d ferens on either side close to the base of the prostate and pass downwards forwards and inwards to open on the posterior wall of the prostatic urethra immediately lateral to the prostatic utricle

The **Ductus Deferens** (*Vas Deferens*) is a long thick walled muscular tube lined with non-ciliated columnar epithelium forming the excretory duct of the testis. Each vas deferens commences at the lower pole of the epididymis, on its inner aspect posterior to the body of the testis pursues at first a slightly tortuous course but soon becomes a straight tube ascending in the spermatic cord where it can readily be recognised from its tactile resemblance to whip-cord. At the internal abdominal ring the vas deferens passes from the posterior to the inner aspect of th spermatic cord and is directed backwards along the external wall of the pelvis towards the inner a pect of the

seminal vesicle The portion of the vas in relation to the seminal vesicle and base of the bladder is dilated and sacculated forming the ampulla the lumen contracting again immediately before it is joined on the outer side at an acute angle by the duct of the seminal vesicle to form the common ejaculatory duct.

The **Epididymis and Testis.**—The testis and epididymis lie within the scrotal sac on either side and are covered by the tunica vaginalis testis a tense bluish white in elastic capsule which dips in between the testis and epididymis to form a well marked sulcus. The epididymis consists of a long highly convoluted muscular tube lined with ciliated columnar epithelium, having an expanded blind upper end the lumen below being continuous with that of the vas deferens. The epididymis lies in relation to the posterior aspect of the body of the testis, and is divided into three parts the globus major or upper part the body or intermediate part and the globus minor or lower part. The globus major is intimately attached to the body of the testis by the vasa efferentia and by the visceral layer of the tunica vaginalis. The inferior extremity of the epididymis is also closely bound to the body of the testis by the tunica vaginalis the intermediate portion being free and only loosely attached by areolar tissue

The **Membranous Urethra.**—The membranous portion of the urethra lies between and pierces the two fascial layers of the urogenital diaphragm to become continuous proximally with the prostatic urethra and distally with the bulbous urethra It is about three-quarters of an inch in length and curves downwards and forwards behind the lower border of the symphysis pubis and with the exception of the meatus is the narrowest part of the urethra. The columnar mucous membrane is scantily supplied with mucous glands, and is directly surrounded by a thin coat of

erectile tissue around which is a layer of involuntary muscle fibre forming the compressor urethræ muscle.

Placed behind and in close relation to the membranous urethra are **Cowper's (bulbo urethral) glands** lying one on each side of the mid line Each gland is a firm round lobulated mass about the size of a small pea and is composed of columnar celled tubules within a fibro-muscular capsule The duct of each gland pierces *the anterior fascial layer of the triangular ligament and* runs forward for about an inch before opening on the floor of the bulbous portion of the urethra.

The **Anterior Urethra**.—The anterior urethra extends from the termination of the membranous urethra to the meatus urinarius on the glans penis It is about six inches in length and is embedded in the substance of the corpus spongiosum penis which expands posteriorly into the bulb. The proximal part of the anterior urethra lying between the anterior layer of the triangular ligament and the penoscrotal junction is termed the bulbous urethra and is about one and a half inches in length This portion of the urethra is fixed in position by its attachment to the triangular ligament and by the suspensory ligament of the penis The distal portion of the urethra is pendulous and mobile Secretions in the pendulous portion of the urethra drain naturally towards the meatus while in the fixed portion they gravitate towards the bulb The anterior urethra is not of uniform calibre being narrowest at the meatus, behind which is a dilatation called the fossa navicularis Behind this the calibre is uniform until the wider bulbous portion is reached

The mucous membrane of the anterior urethra consists of *delicate columnar epithelium except in the fossa navicularis* where it is covered with stratified squamous epithelium continuous with that of the glans. Outside the mucous membrane is the submucous coat consisting of

inner longitudinal and outer circular muscular layers. External to this is a plexus of veins forming part of the corpus spongiosum. The mucous membrane is studded with numerous glandular structures Littré's glands and the lacunæ of Morgagni. Littré's glands are mucus-secreting glands lined with columnar epithelium and are most numerous in the upper or anterior wall of the anterior portion of the urethra but also occur in small numbers on the floor or side walls. The glands are simple, compound, or racemose the openings being directed for ward towards the urethral orifice.

There are also a number of recesses or pockets on the roof and lateral surfaces of the urethra. These are called the lacunæ of Morgagni are blind recesses pointing towards the meatus and are formed by mucosal flaps. The largest of these lacunæ is situated on the roof of the urethra close to the fossa navicularis and is called the lacuna magna or valve of Guérin The ducts of Littré's glands not infrequently open within the lacunæ.

The ducts of Cowper's glands opening on the floor of the bulbous urethra have already been referred to

The lymphatic vessels of the penile portion of the urethra communicate with those of the glans and the other deep lymphatics of the penis to drain to the deep inguinal and external iliac glands. The lymphatic drainage from the bulbar and membranous portions of the urethra is to the internal iliac glands and the inner chain of the external iliac glands.

CHAPTER XIII

DIAGNOSIS AND TREATMENT OF GONORRHŒA IN THE MALE

INCUBATION Period.—An interval which usually varies from four to fourteen days elapses between the time of implantation of the gonococcus on the urethral mucous membrane and the appearance of symptoms and signs of the disease The length of the incubation period depends on factors common to all infections— the virulence and dosage of the organism and the resistance of the infected person. While the incubation period seldom exceeds fourteen days cases do occur in which it may be protracted for as long as eight or even twelve weeks. This more commonly occurs in reinfections Certain local factors predispose to infection in the male of these hypospadias a large meatal orifice and phimosis are the most important.

During the incubation period the gonococcus multiplies and extends along the urethral mucous membrane from the meatus towards the posterior urethra involving successively the anterior urethra and the posterior urethra together with their associated glandular structures and penetrating through the epithelium to the submucous tissues and lymphatics. By the time that symptoms occur the gonococcus is widely disseminated throughout the lower genito-urinary tract

Symptoms and Signs.—Gonococcal urethritis may be symptomless more commonly however some degree of *dysuria* occurs a slight itching or burning on micturition being referred to the tip of the penis and the distal portion of the urethra *Infrequently dysuria is agonising* and

may be associated with nocturnal priapism or chordee. *Increased frequency of micturition* commonly occurs diurnally Nocturnal frequency is less common and suggests involvement of the posterior urethra. *Urethral discharge* commences as a slight mucoid or serous exudate which rapidly becomes purulent or occasionally sanious The lips of the urinary meatus become red swollen and everted, and the urine becomes hazy from the presence of pus or shows a heavy deposit of pus threads. A slight tender enlargement of the inguinal lymph glands may be noted abscess formation is rare.

Physical Examination of the Patient.—While the possi bility of a urethritis is indicated by the symptoms a careful local examination must never be omitted in any suspected case. By careful examination only can other causes of the same symptoms be excluded the true nature of the infection determined and the extent of anatomical in volvement ascertained.

Prior to clinical examination a detailed history must be taken. Enquiry should be made into —

(1) The present symptoms their duration and any treatment applied.

(2) Exposures to infection during the preceding three months.

(3) Previous infections with and treatment for syphilis chancroid or gonorrhœa

(4) Whether the source of infection is known and can be influenced (along with the spouse r other subsequent contacts) to attend for investigation

The patient should be placed in a good light facing the clinician. He should remove his jack t and waistcoat slip the braces off the shoulders and allow the trousers to drop to the ankles. The shirt is then lifted to the level of the nipples The genit lia and xposed skin surfaces are

then inspected and any abnormal appearances noted. The inguinal glands should be palpated.

It is important in the uncircumcised to ascertain whether the discharge complained of is subpreputial or urethral in origin. The prepuce should be retracted, the glans penis and inner aspect of the prepuce are carefully inspected after cleansing with cotton wool swabs moistened in saline. The appropriate investigation is carried out for any subpreputial lesion found.

The urethral meatus is cleansed and inspected and any urethral discharge expressed by gently milking the urethra from behind forwards. The thumb of the left hand is placed at the root of the penis below the pubes with the fingers behind the scrotum. Gentle "stripping" with the fingers along the line of the urethra brings any secretion in the bulbous urethra forward to the penile urethra along which it is milked to the external meatus between the thumb on the dorsum of the penis and the fingers on the ventral aspect. Specimens of the discharge are now taken by means of a sterile platinum loop for smears or cultures.

Palpation of the epididymes, vasa deferentia and other scrotal contents is conveniently carried out between the thumb and the flat of the hand behind the scrotum immediately before "stripping" the bulbous urethra while during the "milking" of the penile urethra. Local complications, for example early peri-urethral abscess or lymphangitis, may be detected.

The anatomical extent of urethral involvement is determined by the *two-glass* or the *three-glass* urine test. In the *two-glass* test the patient is instructed to pass 4 to 6 ounces of urine into a specimen glass and a like amount into a second. The appearance of the first specimen interprets the degree of inflammation of the anterior urethra, while the second indicates whether the posterior urethra is or is

not involved. This test although simple in application is liable to certain fallacies. Incomplete clearance of inflammatory products from the anterior urethra gives rise to haze in the second specimen and may erroneously suggest a posterior urethritis, while conversely the removal of all pus from the posterior urethra by the first specimen of urine voided may erroneously presumptively exclude posterior urethritis. The *three-glass* test is therefore preferable The anterior urethra is washed out with cold, colourless lotion (*e g* saline) by means of a gravity apparatus, until the washings return clear This constitutes the first glass. The patient then voids 4 to 6 ounces of urine into each of two further specimen glasses the contents of the second test-glass indicate the presence or absence of pus in the posterior urethra, while the third specimen shows the state of the bladder urine. It must be remembered that apparent urinary turbidity may result from phosphates and carbonates the routine addition of acetic acid to every urine specimen showing a haze obviates this common source of error The inferences to be drawn from the urine tests are shown in the following table —

TWO GLASS TEST

1st Glass	*2nd Glass*	*Presumption*
Haze (+ pus threads).	Clear	*Anterior urethritis*
Haze (+ pus threads)	Haze (+ pus threads)	*Anterior and posterior urethritis*

THREE GLASS TEST

1st Glass.	*2nd Glass.*	*3rd Glass*	*Presumption*
Haze (+ pus threads)	Clear	Clear	*Anterior urethritis*
Haze (+ pus threads)	Haze.	Clear	*Anterior and posterior urethritis*
Haze (+ pus threads)	Haze	Haze	*Anterior and posterior urethritis and trigonitis*

The urine test shows that the posterior urethra is involved in from seventy to eighty per cent of patients when

then inspected and any abnormal appearances noted. The inguinal glands should be palpated.

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TWO GLASS TEST

1st Glass	2nd Glass	Presumption
Haze (+ pus threads)	Clear	Anterior urethritis
Haze (+ pus threads)	Haze (+ pus threads)	Anterior and posterior urethritis.

THREE GLASS TEST

1st Glass.	2nd Glass.	3rd Glass	Presumption
Haze (+ pus threads)	Clear	Clear	Anterior urethritis
Haze (+ pus thread)	Haze	Clear	Anterior and posterior urethritis
Haze (+ pus thread)	Haze	Haze	Anterior and posterior urethritis and [illegible]

The urine test shows that the posterior urethra is involved in from seventy to eighty per cent. of patients who

they first present themselves for examination Examination of the prostate the seminal vesicles and of Cowper's glands must therefore never be omitted. The patient assumes the knee-elbow position on a couch or stands with the feet separated places the hands on the seat of a chair and bends the body until the head is resting between the hands.

After inspection of the exposed skin area the lubricated



Fig 3
Position of patient for examination of Prostate and Vesicles

gloved forefinger of one hand is introduced into the rectum. A bi-manual examination with the free hand over the pubes greatly facilitates the procedure The *size* of *the prostate its consistence* and *the presence* of the median groove is noted. Any abnormality—general or localised enlargement of one or both lobes irregularity of outline boggy areas or hard nodular areas or areas of undue tenderness—is recorded In the majority of cases the seminal vesicles are normally not palpable If these

can easily be palpated suspicion is raised as to their possible infection.

Movements of the palpating finger to make certain that no area of the prostate is left unexamined are shown in Fig 132

Prostatic massage is carried out in the same manner as examination of the prostate the sole difference being in the degree of pressure exerted by the examining or mas-

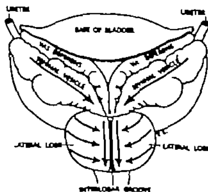


FIG. 132.
Diagram showing movement of finger hen palpating or massaging Prostate and Seminal Vesicles.

saging finger In palpation the pressure exerted should be no more than is sufficient to make out the various features alluded to In massage the pressure exerted should be sufficient to promote drainage from the vesicles prostatic ducts, etc without causing more than slight temporary discomfort to the patient. Prostatic massage must never be carried out in acute anterior or posterior urethritis. Accurate information can, however be obtained as to the state of the prostate and vesicles in subacute or chron c infections by expression and examination of the prostatic

6

and vesicular secretions while it is also of the greatest value in the treatment of these conditions.

The site of Cowper's glands is palpated between the rectal forefinger and the thumb directed successively towards either side of the median raphe of the perineum. Normally Cowper's glands are not palpable but if infected may be felt as tender bodies the size of a pea or larger

The **clinical findings** in a typical case of acute gonorrhoeal urethritis in the male may be summarised —

(1) There is a muco-purulent or purulent urethral discharge which may be milked forward from the deeper portion of the urethra

(2) Redness and ectropion of the urinary meatus are present induration is however absent

(3) There is turbidity of the urines the degree of haze depends on the acuteness of the process and the anatomical extent of infection is indicated by the two-glass or three-glass urine test

(4) Prostatic changes are associated with infection of the posterior urethra.

(5) A secondary balano-posthitis may follow spread of infection from the urethra to the subpreputial sac

(6) Infrequently there is slight tender bilateral inguinal adenitis dorsal lymphangitis or involvement of Cowper's glands

(7) Urethral smears or cultures confirm the presence of the gonococcus.

Differential Diagnosis of Gonococcal Urethritis.—An acute purulent urethritis following sexual exposure leads to the immediate suspicion of probable gonococcal infection Gonorrhoea accounts for from 60 to 80 per cent. of urethral discharges and the other possibilities must therefore be considered in those cases in which the possibility of gonorrhoea is denied by the patient the gonococcus is not demonstrated or when the signs and symptoms are

atypical. Possible causes of urethral discharge fall into several well-defined groups and inability to demonstrate the gonococcus may indicate the necessity of reviewing the case and making enquiries or appropriate investigation into other possible causes.

The causation of urethral discharges may conveniently be considered under the following heads —

(1) Inflammatory
(2) Constitutional
(3) Neoplastic.
(4) Adventitious.
(5) Miscellaneous

Inflammatory —The commoner causes of inflammatory urethritis as seen in clinic practice are tabulated below —

CAUSES OF INFLAMMATORY DISCHARGES.

	Cause of Inflammatory Urethral Discharge	Main Features
(a) *Specific Infection*	*Gonorrhœa*	Purulent urethral discharge Gonococci demonstrable
	Intra meatal or intra urethral *chancre*	Serous or sero purulent urethral discharge. *T pallidum* demonstrable
	Intra-urethral lesions of *secondary* or *tertiary syphilis* (rare)	Serous or sero-purulent urethral discharge *T pallidum* may be demonstrable
	Intra-meatal or intra urethral *chancroid*	Serous to purulent urethral discharge occasionally sanious Pain marked Meatal ulceration may be apparent Gonococcus and *T pallidum* absent Early painful adenitis

	Cause of Inflammatory Urethral Discharge	Main Features
Specific Infections —continued.	*Less common causes* Trichomonatous infestation of urethra	Purulent urethral discharge often associated balano-posthitis Trichomonads demonstrable on dark-ground examination
	Urethral mycoses and *spirochaetosis* (not uncommon tropics)	Muco-purulent urethral discharge — diagnosis by microscopic examination or culture
	Genito-Urinary Tuberculosis	Mucoid or muco-purulent urethral discharge Other organisms often absent Tubercle bacilli demonstrable
(b) *Non-specific Infections*	(1) *Simple urethritis* following sexual exposure causal organisms B Coli staphylococci streptococci enterococci etc	Muco-purulent to purulent urethral discharge causal organism demonstrable Gonococcus absent
	(2) *Stricture* (sequel of previous gonorrhoea) frequently associated with cystitis and non specific urethritis	Watery to muco-purulent urethral discharge Past history and symptoms should suggest necessity for investigation for stricture Gonococci not demonstrable unless re-infection
	(3) Secondary to *urinary tract infection* or disease e g chronic prostatitis, cystitis, pyelitis, pyelo-nephritis, infected hydronephrosis, etc *calculus formation* in bladder ureter kidney—with or without superadded infection	Muco-purulent urethral discharge No microscopic confirmation of gonorrhoea History signs and symptoms should indicate necessary investigation after exclusion of gonorrhoea

	Cause f Inflammatory Urethral Discharge.	Main Features.
(c) Chemical and Thermal.	( ) Use of overstrong or unsuitable antiseptics in prophylaxis or treatment.	Mucoid to muco-purulent urethral discharge. History and details of application h ld gg t se. Organisms often absent microscopically O strong lotions may cause persistence of discharge in treated gonococcal urethritis.
	( ) Id yn ra y to chemical contraceptives	Mucoid urethral discharge. No bacteriological evidence f infection
(d) Traumatic.	( ) Careless, or over frequent instrumentation, indwelling catheter	Muco-purulent to purulent urethral discharge History h ld gg t e. Secondary organisms often present.
	( ) F ign bod es, urethral calculi etc (Mechanical or chemical tissue damage to the urethral mucosa predisposes to pyogenic infection)	Mucoid to purulent urethral discharge, according to degree f secondary fection.

Constitutional.—Certain *physiological* conditions for example oxaluria and phosphaturia may give rise to urethral discharge. This is generally of a mucoid nature but may occasionally be blood stained. Smears show the presence of pus in varying amount and an entire absence of organisms. The occurrence of phosphates in the urine giving rise to a haze which disappears on the addition of acetic acid should, in the absence of bacteria in the smears and cultures suggest the possibility of a phosphaturic urethritis. Oxalates can similarly be demonstrated by microscopic examination of the urinary sediment Allergic

transient mucoid urethral discharges may follow the ingestion of certain foods for example strawberries or asparagus This is probably analogous to the occurrence of urticaria The relation of the onset of the urethral discharge to the ingestion of some special food and the absence of specific bacteriological findings should suggest the diagnosis.

Urethral discharges may occur *in association with systemic diseases* for example acute rheumatism mumps scarlet fever and other exanthemata The discharge is generally mucoid or muco-purulent with a scanty organism content. A purulent urethritis may be associated with typhoid dysentery or influenza In these cases the discharge is secondary to a hæmatogenous infection of the lower urinary tract notably the prostate. In diabetes a mucoid or muco-purulent discharge may occur from sugar irritation of the urethra or from increased growth of normally saprophytic organisms. Itching and local irritation are prominent symptoms and should lead to chemical examination of the urine

Neoplastic.—The urethra may be the seat of simple or malignant tumour formation Warts are not infrequently found on the glans and inner aspect of the prepuce and may extend along the urethra as far as the bulb In some cases the urethra alone is infected The occurrence of a persistent mucoid or muco-purulent discharge in which gonococci are not demonstrated should invariably lead to urethroscopy when the underlying cause is readily apparent The treatment of intra urethral warts or papillomata depends to some extent on their number If they are scanty they may be treated trans-urethroscopically by the electric cautery or by the local application of acid. If they are numerous they should be cut off under direct vision at the level of the mucous membrane by a sharp-edged urethroscopic cannula the urethra being subse-

quently irrigated with 1/500 lactic acid or 1/5000 silver nitrate solution.

Uncomplicated malignant disease of the urethra seldom gives rise to urethral discharge. This only occurs when ulceration and secondary infection take place.

Adventitious.—Sinuses and fistulæ opening into the urethra may cause a urethral discharge

Miscellaneous.—Sexual or alcoholic excesses or masturbation may cause a mucoid or muco-purulent urethral discharge. In many of the cases in which these factors appear to be causal there is an admitted history of previous infection. Careful examination must therefore be made to locate any residual lesions or possible foci of infection which may be lit up by the excess A static urethral discharge may occur in those who are constantly on their feet or who are engaged in heavy work. There is usually a history of antecedent urethritis and examination reveals a subacute prostato-vesiculitis. Prostatorrhœa the expression of opalescent or milky prostatic fluid during defecation may lead to a complaint of urethral discharge The history of discharge occurring only at this time and its absence at all other times should suggest the diagnosis If a smear is obtained little pus is found epithelial cells and mucoid material are present spermatozoa may be present In other cases the findings are those of sub-acute prostatitis

Factitious discharges may be artificially produced to simulate gonorrhœa and to avoid duty The injection of condensed milk into the urethra or the mechanical or chemical irritation of the distal portion of the urethra *e g* by rubbing with the head of a match or by the injection of strong chemicals are commonly favoured methods Microscopic examination of the discharge excludes the possibility of gonococcal infection Urethroscopy may show the site of the lesion to be localised. Artificially produced urethriti involving traumatisation of t

urethra is liable to secondary infection with all the sequelæ of a bacterial urethritis

Bacteriological Confirmation of Diagnosis of Gonorrhœa.—The ultimate proof of a clinical diagnosis of gonorrhœa depends upon the demonstration of the gonococcus in the discharge by the microscopic examination of smears, or by cultures. *The gonococcal complement fixation test is* of value in a number of cases. Bacteriological examination must never be omitted in any suspected case To be successful the greatest care is essential not only in securing specimens for smears or cultures free from contamination, *e.g* from a sub-preputial discharge but equally in the staining and examination

Technique of Making Smears.—A platinum loop is sterilised in a flame and allowed to cool. The prepuce is retracted the external meatus is thoroughly cleansed by moist swabs and finally with spirit The urethra is stripped to bring forward any secretion the lips of the meatus are separated and the specimen is taken from within the meatus by means of the sterile platinum loop. If a smear is to be made the film of pus is spread evenly and thinly over the microscopic slide and is placed aside to dry in the air Alternatively culture tubes or plates may be inoculated

Staining—The only permissible stain for use in the identification of the gonococcus is one of the modifications of Gram's stain Simple aniline dyes for example methylene blue must not be used because of the inaccuracies inherent in the diagnosis solely on the morphological characteristics of organisms

The technique of the commonly employed modification of Gram's stain is —

(1) The slide is fixed by being rapidly passed through a Bunsen flame and allowed to cool

(2) A solution of crystal violet (crystal violet 2 gm

dissolved in 20 c.c. absolute alcohol is added to 80 c.c. of 1 per cent. ammonium oxalate solution) is applied to the smear for 20 or 30 seconds.

(3) The crystal-violet is poured off and the specimen carefully washed with and left covered for 20 to 30 seconds with Lugol's solution (iodine one part potassium iodide two parts distilled water 100 parts)

(4) The preparation is decolorised by washing off the Lugol's solution with acetone the slide being rocked to and fro until decolorisation is complete as shown by the absence of any further violet colour being removed by the addition of more acetone.

(5) The slide is washed in distilled water and the neutral red counterstain (neutral red 1 to 2 gm. 1 per cent glacial acetic acid 2 c.c. distilled water to one litre) applied and allowed to act for one to five minutes.

(6) The preparation is gently washed with distilled water blotted between filter paper and allowed to dry in the air

Alternative counter-stains are aqueous carbol-fuchsin 0 3 per cent. applied for five to ten seconds or 2 per cent safranin applied for a like period

Interpretation of Microscopic Findings.—In films stained by Gram's method the gonococci, being Gram-negative are stained with the neutral red and appear as kidney shaped diplococci with the concave aspects apposed leaving an oval unstained area The size is 1 to 1·6 μ from pole to pole and 0·6 to 0 8 μ in breadth. In the early acute stage gonococci are usually the only organisms present and occur typically clustered within the pus cells, although they may also be found extra-cellularly or attached to the large epithelial cells. Microscopic confirmation of a diagnosis of gonorrhœa is easy during the acute stages with profuse discharge but in cases of old standing urethritis diffi ulties may arise from the scantiness of the gonococci and from the pre ence of other

secondary organisms some of which may morphologically simulate gonococci The difficulties may be increased by hurriedly stained films when for example staphylococci may not have retained Gram's stain or when Gram-positive cocci ingested by the pus cells have lost their affinity for Gram's stain Careful examination is necessary in such cases It will be found that the typical morphology of the gonococcus is lacking, the organisms simulating the gonococcus are larger more spherical and not kidney or bean-shaped like the gonococcus while the characteristic intra-cellular grouping is absent

A single negative microscopic test must not be taken as excluding the possibility of gonococcal infection According to the clinical suspicion in the individual case smears should be repeated at daily or other conveniently short intervals and the probable exclusion of gonorrhœa not assumed until after a minimum of three negative tests. Perhaps the most common cause of failure to demonstrate the gonococcus is because the patient has micturated shortly before the taking of the specimens he should be instructed to retain his urine for at least three hours prior to examination

Cultural Methods.—In cases in which the clinical and microscopical findings are inconclusive the diagnosis of gonococcal infection may be reached by cultivation of the organisms from the urethral secretion or from the centrifugalised urinary deposit Cultural methods should be adopted in those cases especially in women in which the examination of smears has failed to demonstrate the presence of the gonococcus in cases of possible medico-legal significance or when it is necessary to secure complete identification of the organism. While the microscopic findings suffice to confirm the diagnosis in cases in which a discharge occurs after admitted exposure to infection it is impossible to differentiate on morphological

characteristics alone between the gonococcus the micrococcus catarrhalis, the meningococcus or other members of the Neisseria group which may on occasion be found in the urinary tract The gonococcus is a difficult organism to grow especially in primary culture special media are required and the culture tubes should be warmed to 37° C. before inoculation. The media commonly employed are —

(1) Those containing fresh human blood, serum or serous exudate (ascitic or hydrocele fluid)

(2) Those containing fresh animal blood or serum.

(3) Those containing other albuminous products, *e g* egg albumin.

In inoculating the culture tube every care must be taken to secure an uncontaminated specimen of the discharge.

Growth is usually visible in twenty four to forty-eight hours, but may be delayed until the third, fourth or even the sixth day of incubation The colonies are at first small, rounded discrete semi-transparent discs of varying size. Later the margin becomes crenated, the centre becomes thickened and opaque concentric markings and radial striations appear

Absolute proof of this organism being the gonococcus depends on the sugar fermentation tests and on the possibility of (*a*) using the pure culture as an antigen in a complement fixation test against a known gonococcal anti-serum, or (*b*) producing an anti-serum for testing a known gonococcal antigen.

The Gonococcal Complement Fixation Test.—This reaction is closely similar to the Wassermann reaction with the essential difference that the antigen used is constituted from pure cultures of gonococci. While the gonococcal complement fixation test is of considerable value in the investigation of suspected cases of chronic gonorrhœa it has not attained the same reliability or

significance as the Wassermann reaction in syphilis. The reaction is negative for ten or fourteen days following infection and may remain negative during the entire course of uncomplicated gonorrhœa in the male or female. A positive reaction is usually obtained in infection of the posterior urethra in the male and in local or systemic complications in either sex.

After infection has been eradicated the complement fixation test gradually becomes negative in the course of six to eight weeks. The value of the gonococcal complement fixation test may be summed up. A single negative reaction is of no significance in early infection; a positive reaction indicates the possibility of gonococcal infection or of an un-eradicated non-draining focus of infection. In tests of cure a persistently positive reaction indicates the necessity for the most thorough clinical and bacteriological investigation to detect any latent focus. If the tests are consistently negative over a period of six months then cure of the infection may safely be assumed despite a continued positive complement deviation test.

TREATMENT OF ACUTE GONORRHŒA IN THE MALE

The diagnosis of gonorrhœa having been confirmed, appropriate treatment is instituted. The patient should be advised as to (1) the potential seriousness of the disease and the necessity for completion of treatment and tests of cure; (2) the necessity for extreme cleanliness to prevent transfer of infection to the eyes; (3) the avoidance of risks to others by strictly personal use of towel and other toilet articles; and (4) the necessity for the investigation of the source of infection and of other individuals subsequently exposed to the disease. Treatment may conveniently be considered under three headings:—

(1) General. (2) Chemotherapeutic. (3) Local.

General Measures.—In gonorrhœa as in other acute inflammatory infections absolute rest is advisable and if attainable the patient should be confined to bed during the acute stages. If this is impossible all heavy physical work or strenuous exercise is contra indicated. The diet should be non-stimulating avoiding spices pickles and alcohol. The bowels must be carefully regulated. Abundant bland fluids—water tea fruit juices etc.—should be given An alkaline diuretic or a potassium citrate mixture (gr xxx t.d.s.) is of value tincture of belladonna should be added if there is much dysuria. If sulphonamides are to be given strict avoidance of sulphur containing foods, such as eggs and onions is considered no longer necessary Violent purges however especially magnesium sulphate should be avoided.

Chemotherapy—The introduction of the sulphonamide group of drugs and the more recent availability of penicillin have revolutionised the treatment of gonorrhœa rapidly controlling the period of infectivity and shortening the course of the disease. Success in chemotherapy of gonorrhœa depends to a great extent on attention to certain factors —

(1) The accuracy of bacteriological diagnosis and investigation of the anatomical extent of infection.

(2) The maintenance of good drainage from the structures involved.

(3) An adequate dosage of the chosen drug over an adequate time period.

(4) An adequate observation period (tests of cure) to make certain that the infection has been eradicated.

Drugs Employed and the Dosage—The drugs now chiefly employed are sulphapyridine (M & B 693 ") sulphathiazole (M. & B 760 ") and sulphadiazine. While there is little difference in effectiveness between these three drugs the two latter are less productive of toxic sequelæ and are therefore to be preferred.

For ambulant patients a dose of 5 gm. daily for five days is adequate This should be given in three doses, 1½ gm. (3 tablets) after the morning meal 1½ gm after the midday meal, and 2 gm in the evening The tablets should be crushed or chewed and swallowed with a tumblerful of water In hospitalised patients a larger dosage is permissible *e g* 8 7 6 5 5 gm. on successive days.

The mode of action of the sulphonamides is not yet completely understood It is believed that they exert an inhibitory action on the growth of bacteria by interfering with their metabolism and thus render them susceptible to the natural defence mechanism of the body Alcohol tissue trauma or other systemic or local factors tending to inhibit this mechanism may lead to initial failure of the infection to react favourably to sulphonamides, or to later relapse

The sulphonamides show great rapidity of action in the majority of cases the urethral discharge ceases in from one to five days and the smears become pus and organism-free The urinary turbidity usually clears in the same period but a slight haze or threads may persist for a few days longer The cessation of signs and symptoms does not indicate cure surveillance and repeated tests over a period of at least three months are necessary to establish this presumption

Toxic Manifestations following Sulphonamide Administration.—The therapeutic administration of sulphonamides may be followed by certain untoward affect *Nausea vomiting* and *anorexia* result from disturbances to the metabolism of the central nervous system and may be controlled by the administration of abundant fluids potassium citrate (grs xxx q d s) Vitamin C (100 mgm t d.s.) or nicotinic acid (50 mgm. t d.s.)

Cyanosis which was a marked feature of sulphanilamide

administration is now infrequently encountered with the later drugs. The colour is due commonly to the formation of methæmoglobin which does not necessitate cessation of the drug The occurrence of sulphæmoglobinæmia which necessitates immediate stoppage of the sulphonamides is of graver significance. The differentiation between these two causes of cyanosis can only be made spectroscopically

Blood disturbances are not common if courses of sulphonamide administration are limited to 5 or 6 days and separated by an interval of 10 to 21 days. *Acute hæmolytic anæmia* may be sufficiently severe to cause hæmoglobinuria, while prolonged sulphonamide administration may be followed by marked *secondary anæmia thrombocytopenic purpura* or *granulocytopenia* (agranulocytosis) The possibility of blood disturbances should be guarded against by routine hæmatological examination before the administration of further courses of sulphonamides.

Skin eruptions not uncommonly occur after sulphapyridine but are infrequent with sulphathiazole and sulphadiazine Various types of erythematous eruptions—particularly morbilliform—have been observed affecting the skin and the mucous membranes Infrequently exfoliative dermatitis may ensue. The muco-cutaneous eruptions are frequently accompanied by febrile reaction, diarrhœa, arthralgia, splenomegaly and enlargement of the lymph nodes. Skin manifestations not infrequently occur from the 5th to the 15th day after commencement of ulphonamide administration.

Fever.—A rise in temperature to 102 F may occur from the 4th to the 8th day The occurrence of fever without evidence of extension of the original disease or without concomitant signs of muco-cutaneous drug reaction necessitates immediate cessation of the drug The severe toxic conditions of hæmolytic anæmia or l

dyscrasia are not infrequently preceded by temperature reaction. As a rule drug fever falls within 24 to 48 hours of cessation of the drug

Oliguria and hæmaturia may occur from concentration of the urine as it passes down the renal tubules to a point where the solubility of the sulphonamide or its acetylated form is exceeded and precipitation occurs. Hæmaturia concretion formation or tubular obstruction result with consequent oliguria and eventual total urinary suppression.

Visceral damage —Hepatitis with jaundice renal damage simulating the nephrosis of perchloride of mercury poisoning myocardial lesions and encephalopathy have been recorded

The prevention of the toxic sequelæ of sulphonamide administration depends on (1) short intensive courses of administration with adequate time interval between successive courses (2) the administration of large quantities of fluid during the time of sulphonamide administration (3) the control of minor evidences of intolerance by administration of Vitamin C and nicotinic acid and (4) the prevention of major intolerance by routine hæmatological examination before repeating courses of sulphonamide therapy The same measures are of value in the treatment of established cases

Local Treatment.—The rapidity and certainty of action of the sulphonamides in gonorrhœa has relegated local therapy which was previously the mainstay of treatment to a relatively subordinate position Considerable divergence of opinion exists as to whether local measures are necessary in the acute stages of gonococcal urethritis Some authorities adopt the view that these should be instituted only when indicated by the failure of sulphonamides alone Others maintain that the best results follow the combination of sulphonamide with local treatment

which removes the accumulated products of inflammation promotes free drainage from the infected glandular structures and by the local application of heat causes increased blood supply to the area. In cases undergoing penicillin therapy local measures are unnecessary except in the rare event of drug failure.

Local treatment comprises (1) urethral irrigation and (2) special measures, *e g* prostato-vesicular massage, instrumentation or operative procedures. The special measures will be dealt with later under the appropriate complications of male urethritis.

Irrigation of the male urethra is applicable in all stages of urethritis and should invariably be carried out by the gravity method. The hand syringe is an inefficient and frequently septic substitute by which the anterior urethra alone can be cleansed. Its use is followed by a greater incidence of local complications and infection of the urethra with secondary organisms. To carry out the gravity method of urethral irrigation the following utensils are required (1) a douche can of 2 to 4 pint capacity (2) 5 to 6 feet of rubber tubing of suitable size (3) a pinch-clip to occlude the rubber tube and (4) a nozzle of Janet type of glass or vulcanite capable of sterilisation by boiling As an alternative to the douche can a syphon apparatus is available for use with any conveniently sized jug.

The antiseptics most serviceable in acute urethritis are potassium permanganate 1 10,000 to 1 8 000 albargin 1 8,000 or zinc permanganate 1 8,000 to 1 6 000 These dilutions are conveniently prepared by adding the calculated amount of 1 per cent stock solution to the douche can filled with water at 104 to 106 F

Opinions are divided as to whether irrigation of the anterior urethra alone should be practised or urethro-vesical lavage (posterior irrigation) In view of the fact

or	Clinical examination as above smears	(Local treatment ceases unless evidence of persistence of infection)
8 / 5 / 33	Full clinical and bacteriological examination.	Surveillance commences
6	Full clinical and bacteriological examination	—
8[illegible]	Full clinical and bacteriological examination	—
	Final tests full clinical and bacteriological examination. Anterior urethroscopy passage of full-sized, curved metal bougie provocative injection of ½ polyvalent gonococcal vaccine	
	Clinical and bacteriological examinations repeated 24 to 48 hours later	—
	Wassermann reaction or other serological tests to exclude possibility of concomitant syphilis	Surveillance completed

From 60 to 70 per cent of cases treated with adequate dosage of sulphonamides will be found to satisfy these criteria of cure

CAUSES OF PERSISTENCE OF INFECTION

The causes of failure of early gonorrhoeal urethritis to react favourably to adequate sulphonamide therapy fall into one of four well-defined groups —

(1) There is little abatement of the urethral discharge and urinary haze. This may be due to the failure of the patient to take the tablets in the prescribed doses or to egularity in their ingestion. The use of alcohol even in rate quantities inhibits the action of the sulphona- and may lead to complete failure of the chemo-

therapy The avoidance of alcohol is therefore essential not only during the period of, but also for a month subsequent to chemotherapy In a small number of cases in which the previous factors do not occur the anticipated rapid improvement in the urethral discharge does not occur and the possibility of drug fastness of the infecting organism has to be considered. It is still undecided whether these cases are due to a true chemo-resistance of the gonococcus or to some failure of synergic reaction in the tissues of the host. There is some evidence that the latter mechanism is frequently at fault

(2) A scanty mucoid or muco-purulent discharge and some degree of urinary haze or threads persist indicating sub-acute or chronic urethritis. In many of these cases persistence of signs is associated with a non-draining or intermittently draining residual focus of infection in the Littré's gland ducts lacunæ of Morgagni submucous tissues or in the prostate and vesicles.

(3) After a period of apparent cure clinically obvious relapse occurs the signs varying from a slight to a profuse urethral discharge with a varying degree of urinary haze Early relapse *i.e* occurring within one month of the cessation of treatment may be due to the effect of alcohol to the breaking down of a sealed-off focus of infection or to tissue trauma, for example from too early instrumentation or over vigorous prostatic massage. The breaking down of a residual focus of infection may lead to reinfection of the entire urethral canal. Late relapse *i.e* after one month's apparent cure may also occur in these cases the nidus of residual infection is generally in the prostate or vesicles.

(4) Complications occur *e g* epididymitis arthritis or in the female salpingitis, indicating an uneradicated focus of infection.

The treatment of refractory or relapse cases is by the

determination of the anatomical localisation of the persistent focus by the institution of local treatment and by measures designed to increase systematic resistance to the infecting organism.

A careful *clinical examination* and the three-glass urine test will indicate whether the residual lesion is in the structures related to the anterior or posterior urethra in a number of cases both areas are involved. *Urethral irrigation* if not previously instituted, should be commenced. Lavage may suffice mechanically to promote free drainage from the choked glandular structures while the removal of inflammatory exudate the topical antiseptic action and the local hyperæmia consequent upon the use of a warm lotion prevent further extension of the process and materially assist in controlling infection.

The systemic resistance should be augmented by the exhibition of a detoxicated polyvalent gonococcal *vaccine* An initial dose of 0 1 to 0 2 c c. (equivalent to 5 000 to 10 000 million organisms) is followed by gradually increasing dosage twice weekly to a maximum of 1 c.c. (50 000 million organisms) Administration is by intramuscular injection the intravenous route should be adopted in hospital in-patients or out patients able to rest for the subsequent twelve to twenty-four hours. In this latter case the commencing dose should be one-quarter of that for intramuscular injection. The combination of local and vaccine treatment is followed by the rapid disappearance of symptoms and signs in a large number of cases. It is however advisable to give a second course of sulphonamides and preferable to change to a drug other than that used in the initial course In cases responding to this treatment subsequent surveillance should be continued for three months following the same schedule as in primarily successful chemotherapy

Persistence of signs and symptoms or relapse after the

second course of sulphonamides suggests more serious involvement of the urethral structures and indicates the necessity for instrumental investigation of the lower genito-urinary tract and the institution of the special methods of treatment required. The clinical findings and treatment of the lesions found to be responsible for the persistence of gonorrhoea will be considered in the section on Complications.

Penicillin has proved to be highly efficacious as a therapeutic agent in recent gonococcal infections and in long-standing or sulphonamide-resistant cases and is now the drug of choice for routine use. No special preparation of the patient or dietary restriction, except avoidance of alcohol is necessary and no toxic sequelæ except infrequent temperature reactions or urticarial eruptions need by anticipated.

Dosage.—Aqueous solutions of penicillin are more suitable for in-patient treatment a total of 150 000 to 200 000 Oxford units is administered in five equal doses of 30 000 or 40 000 units intramuscularly at three-hourly intervals. For ambulant patients a single dose of 400 000 Oxford units of penicillin in oil-wax emulsion is advised. Penicillin treatment is followed in a few hours by relief of symptoms the urethral discharge becomes less and alters in character from purulent to mucopurulent or mucoid and gonococci cannot be demonstrated. Twenty four hours after treatment no urethral discharge is apparent and at most only a mucoid bead can be expressed by milking the urethra. Smears show little pus but no gonococci. The urine is clear but may show an admixture of mucoid threads which may persist in diminishing amount for several days.

Persistence of a purulent urethral discharge or the demonstration of gonococci in smears taken twenty four hours after treatment should be regarded as a warnin

of possible failure and as an indication for further penicillin administration. A similar course should immediately be repeated In a small number of cases a further course on the third day may be required.

Relapse can occur after apparent cure In general, clinical or bacteriological signs of penicillin failure or relapse-complication e g epididymitis become apparent within two months of cessation of treatment Surveillance should therefore be carried out daily for from seven to ten days then at weekly intervals for the next month, and finally monthly for the following six months. Frequently repeated serological tests are essential during the period of observation for the detection of concomitant syphilis. The dosage of penicillin required to cure gonorrhoea is subcurative in syphilis but is sufficient to delay for several months or prevent the development of the primary sore thus masking the infection until the occurrence of the secondary eruption or positive serological findings. The treatment of relapses following penicillin treatment is by further courses of this drug by sulphonamide therapy by pyrexial measures or by the institution of local treatment

Many clinicians advocate the following up of penicillin therapy by a routine five-day course of sulphonamides, as an additional measure to prevent relapse

CHAPTER XIV

COMPLICATIONS OF URETHRITIS IN MALE LOWER GENITO-URINARY TRACT

THE consideration of the anatomy of the male lower genito-urinary tract enables the clinician to appreciate the possible extensions of infection and indicates the structures in which residual foci of infection may persist and cause protraction of the disease or liability to reinfection of the whole urethral tract. The common sites are —

Anterior Urethra.	(1) The sub-preputial sac the para-urethral ducts Tyson s glands.
	(2) The lacunæ of Morgagni and Littré s glands.
	(3) The sub-mucous connective tissue of any portion of the urethral tract.
	(4) Cowper s glands and ducts.
Posterior Urethra.	(5) The prostatic ducts and the prostate glands common ejaculatory ducts and the seminal vesicles.
	(6) The vasa deferentia and the epididymes.
	(7) The trigone of the bladder and the upper urinary tract

Infected foci in any of these structures cannot in many cases be eliminated solely by local antiseptic irrigations or instillations while the sulphonamides frequently fail to eradicate a closed or intermittently draining residual lesion Local measures are therefore necessary to promote drainage from the infected structures and to permit the successful application of later chemotherapy In cases in

which a profuse purulent urethral discharge continues and there is a marked urinary haze immediate instrumental investigation of the anterior urethra is contra indicated This may cause extension of infection to the posterior urethra exacerbate existing prostato-vesiculitis, or even precipitate metastatic complications. Antiseptic urethral lavage should be continued daily or twice daily until the urethral discharge has become scanty and mucopurulent and the urine in the first test-glass is clear and shows only a flocculate of threads. Investigation of the prostate and vesicles including the examination of prostatic smears should be carried out and any existing infection controlled before investigation of the anterior urethra

It is convenient to consider the possibilities of involvement of the various structures as separate entities, but it must be remembered that more than one may be involved and that there is invariably some degree of concomitant urethritis.

Balano-posthitis.—The sub-preputial sac is lined with squamous epithelium and is resistant to infection by the gonococcus. If however free drainage is impeded by a long phimotic prepuce retention of the purulent discharge containing gonococci sets up a balano-posthitis (see p 351) and predisposes to infection of the para urethral ducts and Tyson s glands

Para-urethral ducts.—Infection of the para-urethral ducts opening on either side of the external urinary meatus, is shown by points of redness at their orifices. On pressure a small drop of pus may be made to exude. The condition is asymptomatic except in cases where the openings are in the urethra immediately proximal to the external meatus when dysuria redness swelling and slight eversion of the meatus may occur The method of choice in eradicating this focus is by complete obliteration

of the duct. A solution of 1 per cent. silver nitrate is injected through a blunt hypodermic or fine-bore silver lachrymal needle introduced as far as possible along the course of the duct. Subsequent careful cleansing of the prepuce, glans penis and the meatal orifice is necessary to prevent re-infection.



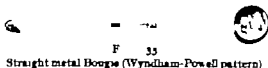
F 34
Abscess of Tyson gland, showing elongated swelling proximal to para-frenal area

Tyson's Glands.—Tyson's glands are situated on either side of the base of the frenum in close association with the coronal sulcus. Infection is usually the sequel of a neglected balano-posthitis. The mouths of the ducts become red and pouting, and pus exudes on pressure. Less frequently abscess formation occurs, giving rise to a localised globular or elongated swelling on one or both sides of the frenum. The treatment of infection of Tyson's glands necessitates the clearing-up of the associated balano-posthitis and the syringing of the duct through a blunt pointed needle with 1 to 4 per cent. mercurochrome solution or 1 per cent. silver nitrate solution. This usually causes rapid cure. Injection may, however, have to be repeated. Abscess formation necessitates incision in the region of the orifice of the gland or in the area of maximum fluctuation and subsequent antiseptic irrigation and fomentations.

Littritis and Lacunitis.—The involvement of the glandular structures related to the anterior urethra (folliculitis) is responsible for the continuance of the symptoms in the majority of cases of persistent urethritis. The amount of discharge and the degree of urinary haze and threads

may vary apparently capriciously from day to day ranging between almost normal findings and those of acute urethritis. Acute infection associated with a purulent discharge marked urinary haze and many heavy pus threads is indistinguishable from acute urethritis.

In subacute and chronic cases urethral discharge may be minimal, but is invariably present on rising in the morning The urine is clear but contains numerous pus threads derived from the gland ducts. These findings may alternate with periods of freedom from all symptoms and



F 35
Straight metal Bougie (Wyndham-Powell pattern)

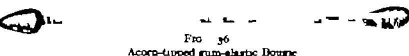


Fig 36
Acorn-tipped gum-elastic Bougie

signs due to the temporary blocking of the openings of the glandular structures with inspissated mucus or pus.

In the florid stages of relapsed gonorrhoeal urethritis, involvement of the glandular structures is inferential, the instrumental investigation necessary to confirm the suspicion being absolutely contra indicated. In the subacute stages when the discharge is scanty the urine shows persistence of threads in the first test-glass and the smears show the presence of pus cells epithelial cells, mucus, and gonococci in varying proportion the degree of involvement of the urethral glandular structures may be accurately determined by exploration with a straight metal bougie an acorn-tipped bougie or by urethroscopy A solid metal straight bougie of the Wyndham-Powell pattern is lubricated and passed with due antiseptic

precautions into the urethra. Palpation of the urethral wall through the corpus spongiosum detects the infected glands as small, hard, rounded, shot like bodies. Alternatively an acorn-tipped gum-elastic bougie may be passed as far as the triangular ligament and slowly withdrawn Non-draining glands are felt as slight obstructions, the patient often experiencing a twinge of pain.

Fig. 37

Mills Section Bougie, straight anterior and curved posterior types, with suction ball, rubber flange to occlude vesical orifice and rubber nozzle to occlude meatus.

The most accurate method of investigating the condition of all the urethral structures is by urethroscopy which permits visual inspection of the mucous membrane and the glandular openings, and reveals lesser degrees of glandular involvement not detectable by the methods previously mentioned. As the cannula is withdrawn from the bulb the infected lacunæ or Littré's gland ducts appear pouting, red and inflamed and exuding pus or muco-pus.



Fig. 38

Kollmann Dilator anterior type with handle

Treatment —The aim of treatment is to establish free drainage from the infected glandular structures. This permits the access of antiseptics to the infected parts facilitates the action of the sulphonamides and prevents possible future abscess formation or extension of the inflammatory process to the peri-glandular or other submucosal structures. The methods of promoting drainage are (1) by massage of the infected glands on a straight metal bougie (2) by the use of Mills's suction

bougie or (3) by dilatation with Kollmann's four-bladed expanding dilator

After irrigating the urethra a full-sized metal bougie is passed the urethra carefully palpated, and the areas of infected glands gently massaged between the bougie and the tip of the finger In the use of a Mills's suction bougie the fenestrated instrument is passed into the urethra and suction made by attaching the rubber bulb emptied by compression between the thumb and fingers. It is necessary to make certain that there is no air leakage at the external meatus. Kollmann's dilator is the instrument of choice in the treatment of folliculitis and of infiltrations The instrument is held in the operator's right hand with the ring finger through the ring on the handle of the instrument After lubrication the dilator is passed along the urethra until the tip reaches the triangular ligament. Separation of the blades is accomplished by gently turning the screw control-wheel between the forefinger and the thumb. The separation of the blades is continued until the patient experiences a sense of tightness or until the clinician finds that the dilator is firmly gripped. This instrument stretches the mucous membrane opens up the mouths of the gland ducts and lacunae, thus loosening the pus plugs and expressing the contents of the glands. By employing a Kollmann's dilator of the irrigating type the urethral surfaces may be constantly bathed with anti-



F 39
Kollmann Dilator use

septic solution. Instrumentation should be carried out at weekly intervals or infrequently twice weekly and must be followed by antiseptic lavage of the urethra. Intermittent dilatation gives ultimately better results than trans-urethroscopic cautery or instrumentation applied directly to the follicles. Urethroscopic treatment is only indicated when a single gland or a few glands in a solitary area are involved. There is no guarantee that the electric cautery or the medicated probe will destroy the entire glandular structure responsible for persistence of infection, while there is the possibility of causing damage to previously uninvolved structures. Progress should be controlled by repeated urethroscopy

Peri-urethral Abscess.—Occlusion of a Littré's gland duct by inflammatory products may lead to a sealed focus



FIG 4
Peri-urethral bscess, pointing subcutaneously in anterior penile urethra

of infection which later breaks down leading to re-infection of the urethra, or progresses to abscess formation. The pus sac gradually increases in size and points towards the mucosa or into the corpus spongiosum The common sites of this occurrence are the fossa navicularis and the bulbous urethra The condition is recognised as a

small tense globular swelling which is tender on pressure and gradually increases in size. When the urethra is encroached on there may be considerable dysuria increased frequency of micturition or distortion of the stream. If the gland duct is still patent an intermittent urethral discharge is noted.



Fig 4
Peri urethral abscess t penoscrotal junction.

Diagnosis —In acute or subacute urethritis the occurrence of a rapidly increasing tender swelling in the corpus spongiosum suggests peri urethral abscess. There may be localised œdema and swelling of the penis which to some extent mask the underlying condition. The passage of a straight bougie into the urethra and careful palpation indicate the nature of the swelling and its relation to the urethra. It may also indicate whether the gland duct is still patent

Treatment —Prevention of peri-urethral abscess depends on ensuring good drainage from the urethral glandular structures in all cases of urethritis When abscess formation occurs the aim should be to encourage rupture into the urethra This may be done after washing out the urethra with antiseptic lotion and instillation of 5 c.c. of 2 per cent novocain which is allowed to act for five minutes by gentle pressure on the peri urethral abscess between the fingers and a straight bougie passed into the urethra. If this does not cause drainage the urethroscope may be passed beyond the site of the abscess, the obturator removed and the visual system attached. Under direct

vision the urethroscopic tube is slowly withdrawn until the wall of the abscess bulges into and fills the lumen of the tube. Air dilatation of the urethra is now relaxed to obviate any risk of air embolism, and free incision is made into the abscess cavity by a sharp-pointed curved bistoury attached to the operating device of the urethroscope or by the electric cautery After incision the urethra is again washed out Subsequent to incision it is important to promote free drainage This is best accomplished by gentle digital pressure daily over the site of abscess formation and by the use of Mills s suction bougie at intervals of three to four days. When the abscess points towards the skin aspiration may be followed by resolution or surgical incision may be required. In aspiration the area of the abscess and surrounding skin is cleansed with soap and water and sterilised with spirit or weak tincture of iodine after which a sharp hypodermic needle is inserted through healthy skin and its point directed to the centre of the abscess cavity A syringe is attached and the contents of the abscess removed by aspiration. The cavity is then washed out with 4 per cent. mercurochrome or a 1 20 aqueous dilution of tincture of iodine. A little of the antiseptic is left behind the needle is withdrawn and the skin puncture is sealed with collodion. Subsequent treatment is by the frequent application of fomentations. Aspiration may require to be repeated daily for three or four days Incision may be followed by the occurrence of a fi tula this however invariably heals with daily packing of the wound

After the abscess has healed and the accompanying urethritis has subsided it is of the utmost importance to investigate the urethra and to deal with any sub-mucous depositions of fibrous tissue which tl erwise may cause stricture formation later

Sub-mucous Infiltration.—Extension of gonococcal in

fection to the sub-mucous tissues leads to the gradual deposition of fibrous tissue (sub-mucous infiltration) which if unrecognised progresses to the establishment of urethral stricture Sub-mucous infiltrations are classified as soft where there is little replacement of the in flammatory exudate by organised fibrous tissue or tran sitional or 'hard as fibrosis progresses. The term 'hard infiltration is synonymous with stricture. While the urethroscope is the only means of diagnosis in many cases a number may be recognised by the feeling of toughened tender patches on withdrawing an acorn tipped bougie.

Sub-mucous infiltrations may occur without concomitant involvement of Littré's glands in other cases the urethroscope shows an irregular deposition of fibrous tissue radiating from these structures. Soft infiltration causes no symptoms or signs if such are present they are due to the associated urethritis or littritis Transitional and hard infiltrations often cause difficulty in the introduction of instruments.

Treatment—The importance of the early recognition of sub-epithelial infiltrations and the institution of treat ment by intermittent dilatation is of the utmost importance in the restoration of the urethra to normal and in the prevention of subsequent stricture formation Dilatation with a Kollmann's dilator should be carried out at weekly intervals. In general absorption of the infiltrate occurs in the course of a few weeks. It is essential to control the progress by repeated urethroscopy

Cowperitis.—The ducts of Cowper's glands open on the floor of the bulbous urethra infection of which is not infrequently followed by extension into Cowper's ducts and glands. Involvement of Cowper's glands is almost invariably followed by occlusion of the duct and abscess formation. Sub-acute or chronic infections of these structures are rare

Symptoms.—In the early stages symptoms are indistinguishable from those of acute inflammation of the bulbous urethra. The patient complains of pain in the perineum especially on rising or sitting down. The pain later extends to the rectum scrotum and inner aspects of the thighs. Reflex frequency of micturition is common and may be troublesome. Less frequently there is pain on defecation or rectal tenesmus.

Diagnosis.—Before the gland abscess has reached any large size the possibility of the symptoms being due to the involvement of Cowper's gland may be missed. Increased frequency of micturition should lead to the rectal examination of the prostate and vesicles and Cowper's glands. The forefinger of the gloved hand is lubricated and introduced into the rectum. The Cowper's gland on either side is palpated between the forefinger and the thumb placed on either side of the median raphe of the perineum. Normally Cowper's gland is not palpable when infected it may be felt as a small, spherical tender body varying in size from that of a pea to that of a small plum.

When abscess formation is marked considerable bulging of the perineum is caused. Rectal examination is necessary to determine whether this condition is due to involvement of Cowper's gland to a peri-urethral abscess or to an abscess tracking from the prostate.

Treatment.—The patient is confined to bed, and the bowels well opened. The lesser degrees of Cowperitis may resolve with hot hip-baths four hourly and applications to the perineum of antiphlogistine or ichthyol and glycerine. If perineal pain is severe and fluctuation is detected the abscess should be incised under local or general anæsthesia. Aspiration has not proved satisfactory. After incision subsequent treatment is by prolonged antiseptic sitz baths and fomentations. Urinary

fistula not infrequently follows incision of a Cowper's abscess. This complication heals up spontaneously if the incision is carefully kept open by daily packing. Sulphonamides may be of value but on the other hand often fail as in other closed foci of infection.



Fig. 4
Spontaneous rupture of bilateral abscess of Cowper Gland

Complications.—If the abscess is not discovered and drained involvement of the posterior urethral wall may lead to extravasation of urine. The abscess may rupture spontaneously into the urethra. It is then liable to become filled with urine emptying slowly between acts of micturition and re-filling. Perineal drainage is essential in these cases. In other cases the abscess may rupture spontaneously through the perineum.

The **posterior urethra** is shown by clinical examination and by the urine glass-test to be involved in between seventy and eighty per cent of gonorrhœal patients when they first present themselves for examination. In the majority of these cases the infection is confined principally to the urethral mucous membrane the glandular structures of the prostate escaping serious implication. When, however the original condition has been neglected or the sulphonamides have proved ineffective infection may extend from the posterior urethra to the prostatic ducts, alveoli and peri-alveolar tissues or through the common ejaculatory ducts and seminal ducts to the vesicles giving rise to acute subacute or chronic inflammatory changes in these structures

Symptoms—Gonococcal infection of the posterior urethra, prostate or seminal vesicles presents a common symptomatology varying in degree from the slightest in cases of simple posterior urethritis to the utmost severity in cases of acute prostatitis prostatic abscess or acute spermato-cystitis Constitutional symptoms increased frequency of micturition pain and apparent decrease of the urethral discharge occur

Constitutional Symptoms—Some degree of general malaise, loss of appetite and interference with sleep is invariable. The temperature may show an evening rise to 100 or 104 F

Increased Frequency of Micturition—The patient is compelled to urinate at intervals varying from an hour or two to every few minutes this increased frequency being especially marked nocturnally The act is accompanied by acute *pain* and *terminal hæmaturia* and its accomplishment is followed by deep cramp-like pain in the neck of the bladder and the urgent desire to recommence the act (vesical tenesmus and strangury) The pain radiates to the perineum along the line of the bulbous urethra to the thighs, back supra-pubic area groins and upwards along the line of the ureters. The amount of *urethral discharge* is apparently reduced because of the frequent urination but also because of the reflux of pus into the bladder giving rise to extreme urinary turbidity *Urinary retention* is commonly associated with prostatic abscess but may occur in any degree of posterior urethral involvement.

While in general the severity of symptoms is in direct relation to the acuteness and extent of the involvement of the posterior urethral structures this is by no means invariably so Gross degrees of prostatic involvement are on occasion almost asymptomatic or markedly acute symptoms are associated with apparently minor palpable

changes in this gland. In any case even the vaguest symptoms suggesting posterior urethral involvement should lead to rectal examination It is important in the digital examination of a presumably acutely inflamed prostatic gland and seminal vesicles that no greater pressure should be exerted than is necessary to make certain of the size and consistency of these structures. Bi-manual palpation with the free hand over the pubes may give rise to a purely temporary sensation of immediate discomfort and pain referred to the tip of the penis.

Acute Prostatitis.—When the extension of acute infection involves the prostatic ducts alone the symptoms and signs are indistinguishable from those of acute posterior urethritis Extension of the process to the prostatic alveoli and peri-alveolar tissues leads to marked inflammatory reaction in the gland

On rectal palpation enlargement of one or both lobes of the prostate is found. This enlargement may be tense tender and of uniform consistence More commonly however the surface of the gland is irregular with definite areas of boggy softening and other areas of hard nodular consistency

Treatment—Rest in bed restriction of diet free purgation the exhibition of large quantities of bland alkaline fluid and cessation of urethral irrigations are essential. Hot hip-baths and hot rectal douching are of value in the relief of pain and in promoting healing The exhibition of morphine suppositories (gr ¼) or atropine (gr 1/75) and antifebrin (gr iv) suppositories may be necessary Retention of urine is usually relieved by insertion of morphine suppositories and instructing the patient to attempt to void urine while in a hot sitz bath If this fails, catheterisation with a soft rubber or gum-elastic catheter should be resorted to after careful urethral lavage with 1 10 000 solution of oxycyanide of mercury After emptying the

bladder should be washed out with the same lotion and a small quantity (ʒi-ii) left behind.

Penicillin and the sulphonamides are rapidly efficacious relieving the symptoms in the majority of cases and causing marked reduction in the size of the gland.

When symptomatic relief has occurred the main indications are to promote free drainage by prostatic massage twice weekly until the prostate has returned to its normal size and consistency. The absence of pus or organisms in the prostatic smears and the clarity of the urine specimen after prostatic massage indicate the eradication of the infection.

The progress of a case should be controlled by frequent bacteriological examination of the urethral and prostatic secretions.

Prostatic Abscess occurs during the course of an acute or subacute prostatitis from occlusion of one or more of the ducts. If this abscess is small the symptoms are indistinguishable from those of acute prostatitis; the close relationship to and pressure on the prostatic urethra may cause greatly increased urinary frequency or acute retention. Usually however the pus sac increases in size forming a large fluctuating swelling involving one or both lobes of the prostate, pressing anteriorly upon the prostatic urethra and bulging posteriorly into the rectum. The local temperature is markedly raised and the rectal wall feels œdematous.

Treatment.—Sulphonamide administration in cases of acute prostatitis prevents abscess formation. In the treatment of an established abscess chemotherapy is less constantly successful but should be instituted. Persistence of symptoms and signs indicating failure of the sulphonamides necessitates treatment directed to the relief of pain and encouraging the abscess to rupture into the posterior urethra. The general measures are as for acute prostatitis; gentle palpation of the prostatic

abscess may cause rupture into the posterior urethra Alternatively this may follow the catheterisation necessary to relieve urinary retention The abscess usually spontaneously ruptures into the posterior urethra within twenty four to forty-eight hours and the patient experiences immediate symptomatic relief Prostatic palpation should subsequently be made daily or on alternate days to ensure free drainage from the abscess cavity when this has satisfactorily contracted the subsequent treatment to complete eradication of infection is similar to that for the resolving stages of acute prostatitis.

While in the majority of cases a prostatic abscess spontaneously ruptures into the posterior urethra in rare instances the abscess points towards and may open into the rectum or rupture may occur into the peri-prostatic tissues. In the former case a rectal gonorrhoea follows and there is the possibility of superadded infection of the prostate by intestinal organisms. Peri-prostatic rupture is followed by a widely diffused perineal and peri rectal abscess. When the danger of rupture of a prostatic abscess into the rectum or into the peri-prostatic tissues is not controlled by the administration of sulphonamides *surgical intervention should not be delayed* The abscess should be opened by the perineal route The anaesthetised patient is placed in the lithotomy position and a curved incision with the convexity pointing forward made through the skin and subcutaneous tissues about one inch in front of the anal orifice The central point of the perineum is defined the transverse perineal muscle is retracted upwards. The fibres of the levator ani muscle are separated by passing sinus forceps through them The wall of the abscess cavity generally presents in this opening and may be incised or punctured with sinus forceps. All loculi should be broken down by digital exploration A rubber drain is now inserted and the perineal wound closed. The

drain is shortened daily and by the end of a week or ten days the perineal wound is permitted to heal. Subsequent to this the treatment follows the same course as for acute prostatitis.

Subacute and Chronic Prostatitis.—These conditions may arise insidiously during the course of a gonococcal urethritis or may follow an acute prostatitis or prostatic abscess.

Symptoms and Signs—The symptoms are frequently vague and not directly suggestive of prostato-vesicular involvement Nervous depression lassitude loss of appetite and weight and impairment of the general health are complained of. The temperature is not raised. Ill-defined pains occur and are referred to the perineum rectum along the line of the lower third of the ureter or the thigh Frequency of micturition is normal or may be increased especially at night. A moderately profuse urethral discharge may be present not uncommonly however this is scanty or intermittent and detectable only in the early morning or when the patient has not urinated for four or six hours. The urine test may show a completely clear specimen in the first glass a flocculate of threads, or a slight haze The second test-glass usually shows clear urine. The portion of urine voided after prostatic massage invariably shows a heavy admixture of comma-shaped prostatic threads, and a ground-glass haze or marked turbidity On rectal examination the prostate is usually found to show some degree of irregular enlargement with localised hard nodular areas, or areas of bogginess. Tenderness of the gland may be marked and generalised confined to localised areas or entirely absent. In some cases an insensitive small fibrotic prostate is felt. Large numbers of pus cells and gonococci can be demonstrated in the expressed prostatic secretion.

Treatment—The course of a subacute or chronic prostatitis depends to a great extent on the amount of

fibrosis which has occurred before treatment is undertaken. The earlier the condition is diagnosed the better is the prospect of speedy cure. Penicillin and the sulphonamides are of great value in eradicating the gonococcus but their administration must be supported by measures to promote free drainage from the prostatic ducts and to increase the local and general resistance of the patient These measures include attention to the general health the administration of a detoxicated gonococcal vaccine hot sitz-baths at as high a temperature as can be tolerated urethro-vesical lavage at a temperature of 105 to 112 F and the institution of prostatic massage Prostatic massage should be continued for not more than six to eight consecutive

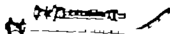


Fig 43
Ultzmann Cannula and Syringe

weeks and if necessary resumed after a rest of fourteen days. This sequence may be continued as long as is necessary Protraction of the condition is often due to persistent obstruction of drainage from the prostatic ducts. This may be remedied by the passage of a curved metal sound of large calibre (24 to 26 French scale) which mechanically stretches the openings of the ducts and facilitates drainage on subsequent prostatic massage A curved Kollmann's dilator may similarly be used or suction applied by means of a curved Mills's fenestrated catheter Alternatively instillation into the prostatic urethra may relieve the blockage An Ultzmann-type *cannula is introduced along the urethra until the tip* reaches the vesical orifice A 5 c c. syringe filled with 1 per cent silver nitrate solution is attached and the contents slowly injected as the cannula is withdrawn. The prostatic urethra will hold three to five c c of lotion and

care should be taken that this amount is instilled before the tip of the cannula is withdrawn beyond the triangular ligament. Instillation of silver nitrate may give rise to some temporary frequency or urgency of micturition this does not persist for more than twelve to twenty four hours. Prostatic massage should be commenced forty eight hours after the instillation.

Acute Spermato-Cystitis.—Acute or subacute involvement of the seminal vesicles may occur at any time during the course of a gonococcal urethritis and is invariably accompanied by some degree of prostatitis and posterior urethritis. It is wiser to regard the prostate and vesicles as one anatomical entity liable to infection and to refer to prostato-vesiculitis rather than to vesiculitis or prostatitis.

Infection of the common ejaculatory ducts and the seminal ducts causes obstruction to free drainage of the vesicle. In the early stages this is due to oedema and swelling of the mucous membrane but later it results from the deposition and contracture of fibrous tissue in and around the walls of the vesicle and along the course of its excretory duct

Symptoms and Signs.—While the symptoms are generally those of a posterior urethritis the accentuation of certain of them suggests vesicular involvement Frequency of micturition is markedly increased, terminal dysuria and hæmaturia is severe fresh blood appearing in the last portion of the urine voided. Painful erections are not uncommon. Pain is frequently referred to the iliac fossa of the affected side and when the right vesicle is involved may simulate appendicitis. An acutely tender distended vesicle is detected on rectal palpation. Involvement is generally unilateral, infrequently it is bilateral.

Treatment —The treatment of acute vesiculitis presents little variation from that for acute prostatitis. Chemotherapy i almost invariably effective in relieving th

acute symptoms and causing marked improvement in the local condition After the acute stage has passed the institution of prostato-vesicular massage is essential to obtain complete resolution of the infection and ensure permanent patency of the seminal and common ejaculatory ducts.

In rare cases acute seminal vesiculitis fails to respond to treatment The persistence of acute symptoms and the rectal palpation of a tense tender distended vesicle indicates the necessity for surgical intervention. *Vasotomy* and the instillation of antiseptics along the vas deferens into the seminal vesicle acts by the introduction of potent antiseptics which sterilise the vesicular contents and by re-establishing normal vesicular drainage Vasotomy may be performed under local or general anaesthesia. After the preparation of the skin an incision one-half to one inch is made along the line of the spermatic cord as it emerges from the external abdominal ring The spermatic cord is made to present in the skin incision by pressure through the back of the scrotum the vas is isolated and fixed by passing a flat director beneath it. A small longitudinal incision is made into its lumen and a blunt pointed cannula introduced. Alternatively puncture may be made with a fine sharp hypodermic needle. A strand of silkworm gut is now passed through the cannula or needle along the vas deferens towards the vesicle for eight or ten inches to make certain that there is no blockage The silkworm gut strand is completely withdrawn and a 10 c c. syringe containing 5 per cent colloidal silver or argyrol is attached to the cannula. Injection of the antiseptic is made slowly after which the syringe is detached the cannula withdrawn the vas deferens reposited in position in the spermatic cord and the skin incision closed Alternatively if further injection is considered desirable the cannula occluded by an obturator is left in position and the vas deferens temporarily fixed

subcutaneously by a skin stitch. The silver solution may be extruded on the next act of micturition or may be retained for several days. After the first instillation has been voided the second may be made. One or two injections generally suffice to control infection and to re-establish natural drainage which must subsequently be maintained by prostato-vesicular massage.

Epididymitis.—Involvement of the vas deferens and epididymis arises from direct extension of gonococcal infection from a posterior urethritis with associated prostato-vesiculitis. Localisation of the infection is predisposed to by trauma, frequently sudden effort or strain by too early or vigorous application of prostato-vesicular massage or by incorrect technique of posterior irrigation. Inflammatory swelling of the vas and epididymis seldom occurs before the second or third week of infection and in sulphonamide treated cases is met with only in refractory or relapsing cases.

Symptoms and Signs.—Premonitory symptoms suggesting the impending involvement of the intra-scrotal structures frequently occur. Pain in the groin localised to the line of the lower third of the ureter or immediately above the inguinal ligament and vaguely radiating along the line of the spermatic cord frequently precedes the inflammatory swelling by twenty-four to forty-eight hours. A vague feeling of weight is felt in the testicle of the affected side. The premonitory signs are gradually replaced by a painful, burning sensation in the lower pole of the epididymis on examination a small hard, acutely tender nodule is detected. In the course of a few hours the inflammatory changes involve the entire epididymis giving rise to a large acutely tender inflammatory mass which may almost completely encircle the body of the testis. The overlying scrotal skin becomes acutely reddened hot and tender and there is frequently su

cutaneous œdema. The symptoms become progressively severe and a temperature of 103 to 104 F may be reached. Urethral discharge becomes scanty or absent. The condition is usually unilateral the left side being the more frequently involved bilateral epididymitis is, however more rare.

The vas deferens may be simultaneously involved and shows a hard rigid acutely tender inflammatory swelling often attaining the thickness of the little finger. The course of the swollen vas may be traced from the epididymis to the external abdominal ring.

Diagnosis.—The occurrence of an acute inflammatory swelling of the epididymis or vas in association with a gonococcal prostato-vesiculitis suggests that the epididymitis is of gonococcal ætiology. Absolute proof can be attained only by demonstrating the gonococcus in the aspirate from the epididymis. The greatest difficulty may be experienced in determining the cause when epididymitis occurs in a partially treated case or when a patient denies any history of antecedent urethritis. In these cases other possible causes of the epididymitis have to be considered (1) direct involvement from non-gonococcal genito-urinary infections *e g* due to *B coli* (2) metastatic infection in association with systemic disease *e g* cerebro-spinal fever (3) tuberculous epididymitis (4) urinary epididymitis unassociated with demonstrable genito-urinary infection due possibly to urinary reflux along the vas and predisposed to by physical effort especially when the bladder is full. Consideration of these possibilities indicates the local general and pathological investigation required in the individual patient.

Lesions of the epididymis may also require to be differentiated from swellings of the testis for example from the orchitis of mumps in whic the associated urethral discharge may on first examin n suggest gor a.

Treatment.—The same dietetic and hygienic rules are applicable as for acute posterior urethritis. Complete rest in bed is advisable for a few days until pain has been relieved and the swelling is diminished. Local treatment apart from a suspensory bandage is seldom required.

Penicillin or sulphonamide therapy is rapidly effective in relieving symptoms and causing resolution of the inflammatory swelling of the epididymis or vas deferens, and should therefore be exhibited in full dosage as soon as the diagnosis of gonorrhoea is confirmed bacteriologically. Not infrequently a fibrous nodule of varying size may be left in the lower pole of the epididymis. Resolution of this nodule is hastened by gently massaging the affected area with iodex or with 5 per cent. ammoniated mercury ointment.

Trigonitis, Cystitis, and Upper Urinary Tract Infection.—In the male gonococcal cystitis is comparatively rare. The squamous epithelium of the bladder is highly resistant to gonococcal infection and involvement only occurs in the presence of a mixed bacterial infection, for example the gonococcus and *B. coli*. The changes are commonly limited to the trigone of the bladder and are seldom generalised.

Signs and Symptoms.—The symptoms are similar to those of posterior urethritis. Supra-pubic tenderness is present in all cases and is associated with a feeling of weight in the pelvis. In the three-glass urine test all portions are turbid, the urine being uniformly blood stained. This contrasts with the terminal bleeding of acute posterior urethritis. The diagnosis is in the majority of cases inferential as the catheterisation necessary to obtain an uncontaminated urine specimen for bacteriological examination is contra-indicated, even after the most careful urethral lavage, by the presence of an acute posterior urethritis.

Treatment.—The treatment does not differ from that for acute posterior urethritis rest a large alkaline fluid intake and the exhibition of sulphonamides, being the main indications.

Pyelitis and Pyelo-Nephritis.—These conditions form the least frequently recognised group of genito-urinary complications of gonorrhoea and may arise from direct extension of infection from gonococcal cystitis or may be metastatic. The gonococcus is rarely solely responsible for the infection secondary organisms staphylococci streptococci and *B coli* are commonly present

Acute or subacute infection of the ureter or of the pelvis of the kidney may occur the symptoms and signs presenting no special features differentiating gonococcal from other pyogenic infections The treatment is as for gonococcal cystitis

Fever Therapy.—The application of pyrexial measures in persistent gonococcal infections of the urethra or in local complications is of the utmost value. When a fever cabinet is available a single session of eight hours at a temperature of 106 to 106·7 F is followed by immediate cessation of symptoms and signs and the infection is *completely eradicated in 90 per cent of cases.* More resistant conditions *e g* arthriti may require from three to seven exposures at five- to seven-day intervals. The technique is similar to that described for neuro-syphilis (p 168) If physical hyperpyrexia is not available a series of fever *is induced by intravenous Pyrifer B coli* vaccine, or T.A.B vaccine local treatment being continued. When vaccine is used it is wise to give a course of sulphonamides at the termination of the fevers.

Penicillin in the dosage already indicated has proved of great value in the treatment of persistent infections and local complications

CHAPTER XV

GONORRHŒA IN THE FEMALE

ANATOMY OF THE FEMALE GENITO-URINARY TRACT

IN the female as in the male, gonococcal infection involves primarily both the urinary and the genital tracts. A knowledge of the anatomy and physiology of the parts is essential to enable the clinician to realise fully the significance of infection.

Anatomy of Female Genito-Urinary Tract.—The external aspect of the female genito-urinary tract is termed the vulva and includes the mons veneris (mons pubis) the labia majora the labia minora, the clitoris the urethral orifice and the vaginal introitus.

The **Mons Veneris** is the prominent rounded pad of adipose tissue lying above and in front of the pubes, the overlying skin being hair-bearing after puberty

The **Labia Majora** are two elevated rounded masses of tissue commencing anteriorly at the mons veneris and extending backwards towards the anus, where they become continuous with the perineum and form the posterior commissure. Externally in the adult they are covered with hair internally they present a smooth surface studded with numerous glands secreting a semi-solid sebaceous secretion

The **Bartholinian Glands** are two racemose mucus-secreting glands, lined with columnar epithelium, situated in the posterior portion of each labium majus. They are surrounded by a firm capsule derived partly from the superficial perineal fascia and partly from the bulbo-cavernous muscle The tortuous duct of each gland runs upward and inwards for about three-quarters of an

to open on the inner aspect of the corresponding labium minus The openings of the ducts are protected by valvular folds of mucous membrane The Bartholinian

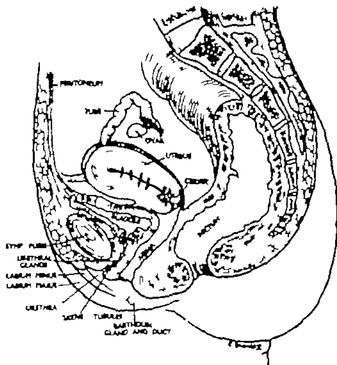


Fig 44
Anatomical diagram of female genito-urinary tract

glands are functionally inactive before puberty and atrophy after the menopause

The **Labia Minora** lie medial to and under cover of the labia majora Anteriorly they form a hood or prepuce for the clitoris From this point they stretch backwards forming triangular folds of tissue containing numerous

sebaceous glands. Posteriorly they fade away into a fold between this fold and the posterior border of the vaginal introitus is a depression known as the fossa navicularis.

The **Clitoris** is the homologue of the penis, presenting a glans and prepuce and forming the apex of the vestibule or triangular area studded with mucus secreting glands bounded laterally by the labia minora and posteriorly by the anterior margin of the vaginal orifice

The **Female Urethra.**—The female urethra commences at the vesical orifice and curves downwards and forwards under the pubic arch, piercing both fascial layers of the urogenital diaphragm in its course to open on the vestibule between the clitoris and the vaginal orifice. Normally the meatus appears as a vertical slit Close to the bladder the mucous membrane is composed of transitional epithelium distally it is of stratified squamous epithelium and contains many gland-follicles and lacunæ. The urethral mucosa is thrown into longitudinal folds by the external muscular coat consisting of outer circular and inner longitudinal layers of muscle and forming the sphincter urethræ. On either side of the urinary meatus are two glandular tubules called Skene's tubules, which open on the floor or sides of the urethra immediately inside the meatus. Occasionally they open directly on the vestibule.

The **Vagina.**—The vaginal introitus is an antero-posterior cleft lying posterior to the urethra and in the virgin is partly occluded by the hymen a thin semilunar fold of mucous membrane with its free border directed forwards, stretching across the posterior half or third of the external vaginal orifice After defloration the position of the hymen is marked by small tags of tissue called the *carunculæ hymenales* The vagina is the passage leading from the vulva to the uterus, is about three inches in length and curves slightly from above downwards and forwards. Normally the anterior and posterior walls are in contact

The vagina is widest at the upper end where the reflection of the mucous membrane on to the cervix uteri forms the fornices. The anterior fornix is in close relation to the base of the bladder the anterior vaginal wall continuing in close contact with this structure and distally with the urethra The posterior fornix extends higher up than the anterior and is in close relation to the recto-vaginal peritoneal pouch (pouch of Douglas) the posterior vaginal wall lower down being in close contact with the rectum On either side is the lateral fornix in close relation to the ureter and uterine artery

The mucous membrane of the vagina is covered with stratified squamous epithelium in the adult and is devoid of glands. The mucous membrane is kept moist by the transudate of serous fluid the reaction of which is highly acid due to the presence of Döderlein s bacillus. In the mid line upon the anterior and posterior walls are two well-defined longitudinal folds the *columnæ rugarum* on either side of which the mucous membrane is thrown into transverse ridges. These rugæ are well marked in the lower part of the canal but are absent higher up External to the mucous coat is a thin layer of erectile tissue beyond which is a muscular coat of internal circular and external longitudinal layers of unstriated muscle fibre

The **Uterus** is a thick pyriform muscular hollow organ *some three inches in length two inches in breadth at its* broadest part and one inch in thickness The broad upper end is directed upwards and forwards resting upon the posterior aspect of the upper part of the bladder the lower end directed downwards and backwards projects into the lumen of the vagina The uterus is suspended from the walls of the pelvis by two peritoneal folds, forming the broad ligament The uterus consists of the *fundus* the upper rounded portion of the body situated above the points of entrance of the uterine (Fallopian)

tubes the *body* that part intervening between the fundus and the *cervix* or neck of the uterus. The cervix uteri is about an inch in length is cylindrical in shape and projects into the cavity of the vagina into which the orifice of the cervix, the os externum uteri, opens. In the nullipara the external os is a round or slightly transverse slit in multipara it is larger and frequently irregular or stellate. The cervical canal is spindle shaped and is lined with columnar epithelium continuous at the external os with the stratified squamous epithelium covering the vaginal portion of the cervix. The mucous membrane of the cavity of the cervix is marked with longitudinal and oblique ridges the *arbor vitæ* the columnar cells on the summit of the rugæ being ciliated The cervical mucous membrane is abundantly supplied with racemose secreting glands, those in the upper part of the canal being lined with columnar cells and those lower down with cubical cells. The cavity of the body of the uterus is lined with ciliated columnar epithelium and is studded with numerous similarly lined simple tubular glands.

The **Fallopian Tubes** (uterine tubes) right and left are about four inches in length and are contained in the superior border of the corresponding broad ligament. Each tube opens into the superior angle of the uterine cavity at the junction of the fundus and the body Proceeding outwards it passes through the uterine wall enters the broad ligament and is directed outwards to the side wall of the pelvis where it arches backwards and pierces the broad ligament to terminate in the fimbriated end communicating with the peritoneal cavity and in close proximity to the ovary The uterine tubes consist of plain muscular tissue arranged in outer longitudinal and inner circular layers and an areolar submucous coat they are lined by ciliated columnar epithelium thrown into longitudinal folds and continuous with that of the

cavity and with the peritoneum at the margins of the fimbriæ.

Lymphatic Drainage from the various areas in the female genitalia can be summarised —

From the vulva to the superficial inguinal glands.

From the lower portion of the vagina to the superficial inguinal glands.

From the middle portion of the vagina to the hypogastric glands.

From the upper portion of the vagina to the external iliac glands.

From the cervix uteri to the glands at the bifurcation of the common iliac artery

CHAPTER XVI

DIAGNOSIS AND TREATMENT OF GONORRHŒA IN THE FEMALE

THE ætiology and incubation period are the same as in the male and while the general principles of history taking clinical examination and treatment follow essentially similar lines, certain modifications are rendered necessary by the different anatomical and physiological considerations in the female The history given by the patient is often unreliable as to exposures to infection, and vague as to the time of onset of symptoms and signs. Comprehensive enquiry should be made into the occurrence and duration of any symptoms and signs suggesting possible infection and any oral or local treatment carried out A complete gynæcological and obstetrical history is of value in indicating other possibilities—uterine displacements, parturition injuries or antecedent inflammatory affections—which might either cause the symptoms or adversely affect the course of a gonococcal infection. Inquiry as to the state of health of the husband or consort should never be omitted

Symptoms and Signs.—In the female the symptoms of gonococcal infection are commonly trivial not infrequently absent, or occasionally severe Some degree of *dysuria* and *increased frequency* of micturition is common urgency *hæmaturia* or *retention* are occasionally complained of A *low backache* over the sacrum is frequent especially in infection of the cervix uteri. There may be some degree of *general ill-health* even early in infection *Alteration in the menstrual rhythm*—menorrhagia metrorrhagia, dysmenorrhœa and the passage of clots of blood

during the menstrual period may occur early in gonococcal infection of the cervix but more frequently indicate involvement of the uterine adnexa The occurrence of *puerperal morbidity* or of *gonococcal ophthalmia neonatorum* may call attention to an asymptomatic maternal infection. Sterility especially *one-child sterility* commonly results from a past unrecognised gonorrhoea A scanty or profuse *vaginal discharge* with or without local irritation is usual. Any combination or degree of the above symptoms may be present In the early stages the symptoms if slight may be ignored until the appearance of local complications, *e g* salpingitis, Bartholinian abscess or systemic extensions, *e g* arthritis.

Clinical Examination of the Female.—The patient should present herself without having previously cleansed the parts and without having voided urine for at least six hours. She should be instructed to arrange her clothing so that the abdomen and pelvic organs may be examined. The lithotomy position is the most convenient and avoids the difficulties and disadvantages of the knee-elbow or Sims s left lateral position In practice the lithotomy position may be obtained by the use of a special table or by asking the patient to sit on the edge of a bed or table to flex the thighs acutely on the abdomen and clasp the front of the ankle joints with the hands. A good light is essential either an angle-poise lamp or a powerful head lamp The stages in examination are —

(1) Palpation of the lower abdomen supra pubic area and inguinal glands.
(2) Inspection of the vulva for evidences of vulvitis vaginal discharge or other abnormal appearances.
(3) The separation of the labia majora inspection of the urethral orifice and vaginal introitus.
(4) Investigation of the urethra.

(5) Palpation of the Bartholinian glands and inspection of the openings of their ducts.
(6) Investigation of the rectum.
(7) Investigation of the cervix uteri.
(8) Bi-manual palpation of the uterus and adnexa.

After palpation of the lower abdomen and inguinal lymph glands the vulva is inspected and any external discharge removed by swabbing with cotton wool swabs moistened in saline or green soap solution. The labia majora are separated by the thumb and finger of the right hand and their inner aspects the labia minora, the urethral orifice and the vaginal introitus inspected after mopping away any discharge.

The middle finger of the left hand is now introduced into the vagina the hand turned palm upwards and the index and ring fingers employed to hold the labia apart. The urethra is palpated through the anterior vaginal wall and any secretion stripped to the external meatus by extension and flexion of the middle finger By partly rotating the left hand the Bartholinian glands on each side are palpated through the posterior third of each labium majus between the middle finger in the vagina and the thumb externally Normally these structures are not palpable but if infected may be felt as globular bodies the size of a pea or larger Any secretion which may be expressed from the Bartholinian glands exudes at the opening of the corresponding duct just outside the lateral margin of the vaginal introitus. The posterior vaginal wall is next stripped downwards and backwards to express through the anal sphincter any exudate which may be present in the rectum. The posterior vaginal wall is now gently but firmly depressed and a Cusco's Brewer's or Ferguson's speculum introduced. If the Cusco type is used the closed blades should be introduced obliquely

through the introitus then turned into the transverse axis and directed along the posterior vaginal wall until the posterior fornix is reached The blades are separated to expose the cervix. After removal by moist swabbing, of any secretion in the posterior fornix or external to the os *the cervix is investigated after which the blades of the* speculum are closed and the instrument is withdrawn. Bi manual palpation of the uterus Fallopian tubes and ovaries is now carried out Any tenderness in the fornices or alteration of consistence of the uterine adnexa is noted.

The primary sites of gonococcal infection are the urethra and the cervix the Bartholinian glands and the rectum are less commonly involved in early cases. Speci *mens of the secretion from these structures should* in turn be collected by a platinum loop for preparation of smears for microscopic examination or for the inoculation of culture tubes

In view of the common association of trichomonas vaginalis infestation with gonorrhœa a routine examina tion should be made for this parasite. A loopful of vaginal secretion from the posterior fornix is diluted with a loopful of saline and a moist slide cover-slip preparation made for immediate dark-ground examination. Alternatively if examination is to be delayed the specimen of secretion may be diluted in saline in a test tube or sealed in a capillary tube

The vaginal acidity (pH) may afford some guide as to the cause of a vaginal discharge. Loopsful of vaginal secretion may be applied to nitrazin testing paper or other universal indicator the pH being determined by comparison with a standard scale Alternatively a special pipette may be used to dilute the vaginal secretion with saline and collect a large specimen for later examination The speculum and other instruments used must be dry

and uncontaminated by any lubricant which might cause alteration of the vaginal pH

Provocation.—Considerable difficulty is not infrequently experienced in demonstrating the gonococcus in the urethral or cervical secretions. Provocative applications are made as a routine—glycerine ½ per cent. pilocarpine nitrate, or 1 to 5 per cent. silver nitrate. The selected application is painted over the mucous membrane of the endocervix and urethra by means of a probe dressed with cotton wool. This increases the amount of local secretion and facilitates and increases drainage from the glandular structures. Re-examination and collection of further specimens for pathological examination should be carried out twenty-four hours after the provocative application.

In the event of the gonococcus not being demonstrated on the first examination tests should be repeated daily for two further days and then at the end of the week. Blood should be taken at the time of the first examination for a Wassermann reaction or other serological test for the exclusion of syphilis.

Clinical Findings.—The local appearances in gonococcal infection in the female vary as greatly as do the symptoms. An apparently normal appearance of all structures is not incompatible with a recent or chronic gonococcal infection; more commonly however some definite inflammatory signs are present —

(1) *Vulva*.—There is usually some degree of mucopurulent vulval discharge unaccompanied by gross alteration of the skin or mucosal surfaces. Infrequently an acute vulvitis associated with profuse discharge, marked reddening and excoriation of the epithelium and inflammatory oedema of the labia majora and minora is present.

(2) *Urethra*.—The urethra is invariably involved in gonococcal infection in the female. Dysuria varying from

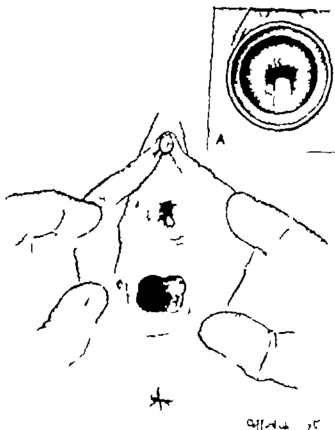


FIG 45

A T GON RRHŒA TH I MALE

Composit picture showing ( ) flammatory swelling f labia minora ( ) redness and swelling f urethral me tus, w th eversion of mucosa, purulent discharge nd nfection of Skene t bules (3) prominent *infected crypts in vest bule (4) nfection of right Bartholinian duct,* redness of orifice and extrus g bead of pus (gonococcal macule ")

Inset View of the ervi show ng acute flammatory central erosion, fad g peripherally t normal tissue and prom of viscid pus

a slight sense of discomfort to scalding pain and increased frequency or urgency of micturition occur In acute infections the mucous membrane of the urethral meatus is swollen congested and everted. A slight or profuse muco-purulent or purulent discharge is seen to exude or may easily be expressed by stripping the urethra. The whole area is exquisitely tender on palpation. The orifice of Skene's ducts may be visible as angry red points pressure through the anterior vaginal wall bringing a small bead of pus to their orifices The urine is turbid.

(3) *Vagina* —The vagina invariably shows some degree of muco-purulent or purulent discharge. The mucous membrane may appear normal throughout commonly however there is a localised inflammatory vaginitis of the posterior fornix. An acute generalised vaginitis is less usual. The vaginal surface appears red and œdematous and there is marked epithelial desquamation

(4) *Cervix* —In acute infections the cervix shows generalised œdema and congestion, and may bleed easily on examination The external os is everted and is surrounded by an acute angry red erosion resulting from destruction of the stratified squamous epithelium of the vaginal portion of the cervix.

If the acute stage has passed and the patient has entered into the subacute stage before examination is carried out symptoms may be entirely absent and the clinical appearances quite normal although gonococci can be demonstrated in smears or cultures Commonly however some evidences of infection exist. The urethral orifice appears normal but a scanty mucoid or muco-purulent discharge can be expressed. A muco-purulent vaginal discharge i common the amount varying within very wide limits Subacute inflammatory changes of the vaginal mucous membrane are localised to the posterior fornix. The cervix frequently shows a chronic erosion

the presence of Nabothian follicles indicating partial healing. A mucoid or muco-purulent endocervical discharge is found.

Diagnosis.—The symptoms—dysuria, frequency of micturition, local pain or irritation, and the signs—vaginal discharge—suggest the possibility of gonococcal infection. The same syndrome, however, follows infection with other pyogenic organisms, while vaginal discharge, frequently the sole complaint, may be due to many and varied causes. These fall into the same groups as in the male, namely (1) inflammatory, (2) constitutional, (3) neoplastic, (4) adventitious, and (5) miscellaneous.

The possible causes of inflammatory vaginal discharges may be tabulated:—

INFLAMMATORY VAGINAL DISCHARGES

	Possible Causation
(a) *Specific infection*	Gonorrhoea Lesions of primary, secondary or tertiary syphilis Chancroid Trichomonatous vaginitis. Vaginal thrush Tuberculous infection } Rare Diphtheria } Rare
(b) *Non-specific infection*	Pyogenic organisms, e.g.— B. coli Enterococci, etc.
(c) *Traumatic*	*Foreign Bodies*— e.g. Ring pessaries Cervical or intra-uterine contraceptive appliances Foreign bodies accidentally introduced Retained internal sanitary pads *Chemical*— Chemical contraceptives Overstrong antiseptic douches.

The enumeration of these possible causes of inflammatory vaginal discharge sufficiently indicates the scope of interrogation and the clinical investigation which may be necessary to reach a diagnosis in any individual case. The main points in differentiation between certain of the commoner causes are tabulated on pages 292 and 293

Constitutional.—*Physiological leucorrhœas* may occur as for example in association with excess of œstrin secretion. The discharge is mucoid and contains few pus cells the vaginal mucous membrane presents a healthy rather thickened pearly appearance.

Pathological changes following physiological processes *e.g* cervical lacerations and uterine displacements may cause a mechanical leucorrhœa or predispose to non-specific infection. Post-menopausal vaginal discharges may result from senile vaginitis or senile metritis.

During the course of *systemic disease e g* scarlatina or the other exanthemata vaginal discharges of mucoid muco-purulent or purulent character may result from metastatic infection. *Anæmia overwork pelvic congestion* from constipation, or threadworm infestation of the bowel are frequently causal or aggravating factors.

Neoplastic.—Non-ulcerating, benign or malignant growths of the vulva vagina or cervix *e g* warts polypi etc. cause a serous or mucoid discharge sloughing benign tumours *e.g* a sloughing cervical polypus or ulcerating malignant growths *e g* cervical carcinoma give rise to a sanious, offensive irritating discharge.

Adventitious.—Vaginal discharge may result from sinuses and fistulæ *e.g* vesico-vaginal or recto-vaginal fistulæ

Miscellaneous.—A static vaginal discharge occurs in those constantly on their feet *e g* overworked waitresses constipation and anæmia are frequent but by no means invariable concomitant factors.

DIFFERENTIAL DIA NOSIS C NO CAUSES INFLAMMATO Y V INAL DISCHARGES

	4 atomi al Areas I volved	Cl ical Appearanc	Vaginal Acidity	Doderlei Bacillus	Co firmat on f Diagnosis
Gonococcal I fection	Urethra Endocervix B th l gland Rectum	Urethritis, rethral dis harge V ginitis localised to posterior vaginal fornix or generalised vaginal discharge Endocervicitis cervical erosion cervical discharge purulen or muco purulent	U ually lo pH 6–8 m y be normal (4 4 5) early infection	Present early nfection Absent later	Gonococci demon strable by smears or cultures in secretion from sites of infection. Complement fixation test may be positiv
Trichomonatous Vagi it	V gina V gi al portion of cer Urethra often unaffected	Ra beef ppear ance f or tra berry patches on gual mucosa Froth muco purulent vaginal discharge Cha ges do not oh endocerv	Lo pH 6 or nder	Absent	Trichomonas Vaginalis (T V) demonstrable by dark-ground xamin tion smears or cul tures (May be associ ted with gonorrhoea and gonococcus demon strable only after T V nfestation controlled by treatment)

	Anatomical Areas Involved	*Clinical Appearances.*	*Vaginal Acidity*	*Döderlein Bacillus*	*Confirmation of Diagnosis.*
Vaginal Thrush.	Vulval skin or mucosa. Vagina. Vaginal portion of cervix. Peri-vulval skin.	Vaginal discharge scanty frequently caseous or unpigmented secretion. White curdy patches on vagina, &c. Signs often trivial in relation to severity of itching.	Highly acid pH 4–4.5.	Present in large numbers.	Gonococcus absent. Oidium albicans easily demonstrable.
Non-specific Infection.	Urethra. Endocervix. Bartholin glands.	Urethritis with varying degree of discharge. Endocervicitis commonly with chronic cervical erosion, and scanty or profuse discharge. Varying degree of vaginitis with frequently profuse muco-purulent or purulent discharge.	Low pH 6.	Absent.	Absence of gonococcus on repeated examination. One organism may predominate, e.g. enterococcus. Non-specific infection may co-exist with T.V. infestation.

The ultimate diagnosis of gonococcal infection in the female depends upon —

(1) The history of exposure to infection

(2) The symptoms and clinical appearances.

(3) The demonstration of the gonococcus in smears or cultures made from the secretions of the urethra, cervix Bartholinian glands and rectum (page 236)

(4) The gonococcal complement fixation test (page 239)

In spite of a suggestive history and clinical findings considerable difficulty is not infrequently experienced in demonstrating the gonococcus microscopically especially if the patient has been using antiseptic douches or if even small doses of sulphonamide have been ingested.

In these cases cultures are of the greatest aid in establishing the diagnosis. In general the earlier after infection the patient is investigated bacteriologically the easier is the demonstration of the gonococcus. Provisional exclusion of gonococcal infection should not be assumed until after a series of three to five negative tests has been obtained over a period of fourteen days. Complete exclusion of infection necessitates observation over a period of three months.

Treatment.—Advice as to the implications of the disease the necessary precautions to be adopted and the general measures are similar to those advised for infection in the male. A daily sitz-bath is advisable during the menstrual period. Alternatively liquor sedans (B P) ʒi q d.s. should be given during this time

Chemotherapy—The principles of sulphonamide or penicillin administration and the dosage are the same as for the male (pages 241 and 251)

Local Treatment.—Many authorities consider that chemotherapy alone is sufficient in recent gonococcal infections in the female. Local measures are however frequently required to clear up residual cervical erosions

or persistent discharge. The aim of local treatment is to promote drainage from the sites of infection especially from the associated glandular structures, and to inhibit the gonococcus by topical antiseptic applications. Vaginal douching, although cleansing the vagina of the gross products of inflammation and promoting the local comfort of the patient does not deal effectively with the foci of infection in the endocervix and urethra. The use of douches should therefore be avoided except when local tenderness or inability of the patient to attend prevents the adoption of other measures.



FIG. 46

Harrison back-flow cervical irrigator

Effective treatment of the urethra and cervix may be wet or dry and is carried out in the lithotomy position. In wet treatment after cleansing of the vulva, the urethra and bladder are irrigated as in the male using a Janet type nozzle with a shield to prevent the splashing of the operator A vaginal speculum is then passed and the cervix brought into view and after cleansing the vaginal mucous membrane, the cervical canal is washed out through a back flow irrigator The lotions commonly used are potassium permanganate albargin or zinc permanganate in similar dilution and at the same temperature as for the male. The vagina is mopped dry and a gauze pack moistened with glycerine, boro-glycerine or ichthyol and glycerine (5 to 10 per cent.) inserted. This treatment should be carried out once daily during the

acute stages and reduced in frequency as improvement occurs.

In dry treatment irrigation of the urethra and cervical canal is not employed. The bladder should first be emptied. After cleansing the vulva with sodium bicarbonate or dilute green soap solution the urethral canal is mopped dry and the chosen antiseptic applied along its entire length by means of probe sticks dressed with cotton wool. A vaginal speculum is now passed, and any inflammatory products removed by moist swabbing, the areas then being mopped dry. The endocervix is similarly treated, first by moist dressed probes to remove the secretion, then dried, and the antiseptic application made. Finally the vaginal portion of the cervix, the fornices and the vaginal walls are heavily insufflated with dusting powder (zinc oxid ʒi, bismuth subgall. ʒii, magnesii carb lev ʒii, pulv amyli ad ʒi) as the speculum is being withdrawn.

The antiseptics commonly used are 10 per cent ichthyol in glycerine, 2 to 5 per cent mercurochrome in glycerine or aqueous solution, 1 to 5 per cent silver nitrate solution, or 1 per cent picric acid solution. Alternatively colloidal silver preparations, 5 to 10 per cent protargol or argyrol, or gonopar* may be employed. Gonopar is semi-fluid at body temperature and is best injected into the urethra and cervix in amounts of 1 to 2 c.c. by means of a record syringe and suitable cannula. Treatment should be carried out daily or at longer intervals according to the indication of the individual case.

In sub-acute cervicitis or in the treatment of residual lesions, e.g. cervical erosions, stronger antiseptic applications having a cauterising action are permissible, e.g. 10

* Research Products, London. The formula of gonopar is —paraff liq. [illegible] parts, paraff moll. [illegible] part, hexyl resorcinol [illegible], sodium ricinoleate [illegible]000, colloidal silver [illegible]000.

per cent. picric acid in alcohol 10 to 15 per cent silver nitrate solution or weak tincture of iodine. These should be applied not more frequently than once weekly Persistence of a cervical erosion associated with discharge may necessitate the application of medical diathermy dilatation and curettage or linear diathermic cauterisation before healing is achieved.

The schedule of the course of uncomplicated gonorrhœa in the female reacting favourably to sulphonamide therapy is comparable to that outlined for the male After completion of chemotherapy and local treatment observation should be continued at weekly intervals for four weeks fortnightly for the next four weeks, and then after the completion of the menstrual period for the next four months. On each occasion there should be a complete clinical examination with collection of specimens of secretion from the urethra and cervix and if available from the Bartholinian glands and rectum for microscopic or cultural investigation. A blood Wassermann reaction or other serological test for the exclusion of syphilis should be repeated at the time of the final tests.

The criteria of cure of gonorrhœa in the female may be summarised —

(1) Absence of signs and symptoms.
(2) Normal clinical findings
(3) Absence of gonococci and pus from urethral and cervical smears.
(4) Negative cultures.
(5) Negative gonococcal complement fixation test
(6) Period of observation—six months.

During the period of surveillance the patient should have no treatment and after the end of the first month should lead a normal life as regards diet exercise alcohol etc. Provocation may be carried out with pilocarpine nitrate or silver nitrate locally or by the subcutaneous

injection of ½ to ¼ c.c. polyvalent gonococcal vaccine equivalent to 300–500 million organisms twenty-four to forty-eight hours before taking the specimens for bacteriological examination. The gonococcal complement fixation test if positive in the early stages of the disease should be negative at the end of treatment or gradually become so during the course of observation (the effect of provocative vaccine injections must be borne in mind)

In many cases it may be impossible to carry out these stringent tests of cure, but if the intelligent patient is advised as to the reasons necessitating long surveillance despite apparent cure little difficulty is met with in securing full co-operation and regular attendance

The causes of persistence of infection and the measures primarily to be adopted are similar to those in the male.

COMPLICATIONS

Urethra.—Persistence of urethritis may be due to involvement of the urethral glandular structures or to subepithelial infiltration Skene's tubules frequently persist as foci of infection intermittently filling up and discharging their contents and causing reinfection of the urethra. Apart from the persistence of urethritis Skenitis may give rise to no signs When the urethral meatus is separated by a Dawson's speculum the openings of the gland ducts are seen to be red and inflamed and on pressure through the anterior vaginal wall may exude a small quantity of pus. Treatment is by injection of 1 per cent silver nitrate or 4 per cent mercurochrome solution by means of a fine blunt-pointed cannula This obliterates the ducts. Per

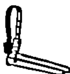


Fig 47 Dawson urethral speculum

sistence of infection in the other glandular structures of the urethra and submucous infiltrations are treated by dilatation with Kollmann's dilator as in the male. Peri urethral abscess may occur. Stricture of the female urethra is comparatively rare, but may be responsible for frequency of micturition, retention of urine, pyuria or later calculus formation.

Bartholinitis.—Infection of the Bartholinian ducts and glands may occur at any time during the course of a gonorrhœa. Infection is usually unilateral, the gland on the left side being more frequently involved. Infection of the gland duct is followed by occlusion, the organisms pressing backwards to the gland and leading to suppuration and abscess formation. Involvement of the duct is shown by the red inflammatory appearance of its orifice and by the expression on pressure over the gland of purulent or muco-purulent secretion. Local pain and increased frequency of urination are constant symptoms. Abscess formation causes a well-defined acute inflammatory tender swelling which can be palpated in the posterior third or half of the corresponding labium majus. Abscess formation is distinguished by the pain and local tenderness from a Bartholinian cyst, and by the localised nature of the swelling from the lymphangitic œdema accompanying a primary sore of the labium.

Diagnosis.—The occurrence during the course of a gonorrhœa of an acute inflammatory swelling suggests an acute Bartholinitis with or without abscess formation. Confirmation of the ætiology is by demonstration of the gonococcus in the gland secretions.

Treatment.—Penicillin and the sulphonamides are of value in relieving the symptoms and in many cases entirely cure the condition. On the other hand, in some cases, especially those of closed abscess formation, they may prove ineffective. Local measures should therefore be

applied to supplement the chemotherapy Prolonged sitz baths at a temperature as high as can be tolerated by the patient should be given once or twice daily If the Bartholinian duct is obviously patent or if slight pressure over the gland frees the blockage treatment by instillation is the method of choice. The contents of the abscess cavity are expressed by gentle pressure over the Bartholinian gland the duct is catheterised with a fine blunt-pointed cannula (*e g* a silver lachrymal needle) and 4 per cent. mercurochrome in glycerine or water injected. Alternatively colloidal silver preparations may be used. Instillation should if necessary be repeated daily or at longer intervals until the infection is eradicated. If the duct is occluded the abscess should be aspirated using a wide-bore exploring needle The cavity is subsequently injected with mercurochrome-glycerine solution before the needle is withdrawn. A slight leakage of the antiseptic through the puncture may occur subsequently permanent sinus formation is rare This procedure may have to be repeated on two or three occasions before cure results

Surgical incision is required when the abscess points towards the integument or when spontaneous rupture leads to tracking of the pus posteriorly towards the perineum or anteriorly along the tissues of the labium. Chronic infection and the persistence of sinuses are indications for surgical excision of the gland.

Endometritis and **Metritis.**—Acute endometritis is not often met with despite the close relationship between the cavity of the uterus and the endocervical canal It is probable that in a number of instances the occurrence of endometritis is masked by the signs and symptoms of the accompanying cervicitis or salpingitis. In acute endometritis there is marked rise in temperature general malaise nausea and vomiting and a dull or sharp ache over the sacrum and supra pubic area On vaginal examination

the uterus is found to be a little enlarged and markedly tender There is a profuse cervical discharge, thinner and less tenacious than in cervical infection alone and not infrequently sanious. An acute cervical erosion is invariably present.

In subacute endometritis the symptoms are less marked menstrual dysfunction is frequent and is indicated by dysmenorrhœa, menorrhagia, or metrorrhagia. There is a profuse thin cervical discharge and cervical erosion the uterus is slightly enlarged and tender Some degree of metritis invariably co-exists with acute or sub-acute endometritis. Treatment is primarily by rest in bed and sulphonamide or penicillin therapy

Salpingitis.—Infection of the Fallopian tubes may occur at any time during the course of a gonococcal infection from direct extension of disease from the endocervix. Possible involvement of the uterine adnexa is frequently indicated by vague premonitory signs—marked pain at the menstrual period menorrhagia or metrorrhagia, and the passage of blood clots. The onset of acute salpingitis is accompanied by a severe generalised pain in the lower abdomen and a sharp rise in temperature to 102 to 103 F The patient looks and feels acutely ill nausea and vomiting are frequent. On abdominal examination marked tenderness and increased muscular rigidity of the lower abdomen are noted The tenderness is most marked in the iliac fossæ and supra-pubic region or low down immediately above the inguinal ligaments. The pain is frequently of an intermittent colic like nature with a tendency to radiate to the vulva. On bi-manual examination the uterus feels tender and is frequently enlarged there is acute tenderness in one or both lateral fornices according to whether the involvement of the uterine tubes is unilateral or bilateral. In the early stages no definite swelling can be palpated through the lateral fornices

in the course of a few days definite tubal swelling can be made out.

Diagnosis.—Salpingitis is suggested by the occurrence of acute abdominal symptoms in association with signs and symptoms suggesting gonococcal infection. It must be differentiated from acute appendicitis. In the latter there is a sequence of central abdominal pain, vomiting, and localisation of pain to the right iliac fossa higher up than in salpingitis. The temperature is not raised. In salpingitis vaginal examination elicits uterine swelling and tenderness, tenderness in both fornices with diffuse swelling or a definite inflammatory mass. In appendicitis, except where the organ is in the pelvic position, vaginal examination reveals no local tenderness.

Treatment.—Rest in bed and sulphonamide or penicillin administration invariably cuts short the complication and other treatment is seldom required. After completion of treatment of any residual lesions, *e.g.* in the cervix, and subsequent surveillance, tubal inflation should be carried out to make certain that the patency of the tubes has been restored.

Pelvic Peritonitis.—The peritoneum is frequently involved by the spread of gonococcal infection from the uterine tubes. Usually the peritonitis is localised to the pelvis and may be inferred from the more widespread character of the pain and difficulty in passing urine and fæces. The symptoms are often masked by the accompanying salpingitis. Generalised infection of the peritoneal cavity rarely occurs in gonorrhœa.

CHAPTER XVII

GONOCOCCAL PROCTITIS METASTATIC COMPLICATIONS OF GONORRHŒA MUCO-CUTANEOUS MANIFESTATIONS OF GONORRHOEA

GONOCOCCAL PROCTITIS

GONOCOCCAL infection of the anal canal and of the rectum is not infrequent in adult women and in association with the vulvo-vaginitis of pre-pubertal girls but occurs less commonly in males. In the female the majority of cases follow direct extension of infection from a genital gonorrhœa in men the condition may follow the rupture of a prostatic abscess, an abscess of Cowper's gland, a posterior peri-urethral abscess or less frequently sodomy

Symptoms and Signs —The condition is not infrequently asymptomatic and may be detected only on careful routine examination. In many cases however itching and a feeling of irritation round the anal orifice are complained of. Formication may extend widely over the inner aspect of the buttocks and perineum and rectal tenesmus may occur Examination may reveal no apparent external signs usually however there is some degree of peri-anal inflammation and a slight or profuse muco-purulent discharge exudes or can be expressed from the anus

Diagnosis —The occurrence during the course of a gonococcal infection of even vague symptoms referable to the rectum should lead to a careful local examination and to the bacteriological examination of any discharge The ultimate confirmation of a diagnosis of gonococcal proctitis depends on the demonstration of the gonococcus.

Treatment—Penicillin and the sulphonamides are by no means invariably successful in eradicating a gonococcal proctitis and in view of the possibility of genital reinfection from this source it is essential that local treatment should be applied as a routine. In the acute stages daily irrigation with 1/5000 potassium permanganate or 1/2000 mercurochrome solution should be made and followed by the introduction of a protargol suppository In more chronic cases where the condition has not been recognised until infiltration of the submucous tissues has occurred treatment should be carried out through a proctoscope, and all the involved areas directly treated by the topical application of antiseptics.

In the majority of cases treatment is uneventful and the condition rapidly clears up Infrequently however ulceration of the mucous membrane fissure in ano or peri-anal abscess formation occurs, while if the condition has persisted untreated for any length of time submucous infiltration may lead to rectal stricture Treatment is on general surgical principles after the appropriate measures have been taken to control the gonococcal infection

METASTATIC COMPLICATIONS

Gonorrhœa usually remains a localised genito-urinary disease In certain cases however especially those with acute or chronic involvement of the prostate and vesicles in the male or of the cervix and uterine tubes in the female the gonococcus may enter the blood stream and cause metastatic infection of other structures. Toxic conjunctivitis iritis and involvement of the joints are the common metastatic lesions more rarely the periosteum ligaments, muscles tendon sheaths, endocardium pleura, or meninges are affected

Teno-synovitis and Bursitis.—Involvement of the tendon sheaths and bursæ may occur at any time during the course of a gonococcal infection as a solitary metastasis, or in association with arthritis. The extensor tendons of the arm or leg, the Achilles tendon, the ligamentum nuchæ or the tendons in relation to affected joints are commonly involved. The onset may be sudden and acute and characterised by swelling redness, and tenderness along the course of the affected tendons voluntary movements being restricted by pain or slow and insidious involvement being shown by a coarse crepitus on movement, palpable along the course of the affected tendon sheaths and by mechanical restriction of movement.

Bursitis is rare except in association with arthritis. The *supra patellar and pre-patellar bursæ of the knee*-joint and the bursæ in relation to the tendo Achilles are not infrequently involved. The symptoms and signs are similar to those of acute bursitis from other causes.

Gonococcal involvement of the *plantar fascia* leading to flat foot is not uncommon. In the early stages pain is referred to the plantar arch especially on standing On examination, œdema of the sole of the foot is found with diffuse tenderness along the course of the plantar ligament. An exostosis at its calcanean attachment (calcanean spur) may form.

Arthritis.—The joints are liable to metastatic involvement at any time during the course of gonorrhœa in the male or female these manifestations commonly occur about the third or fourth week of untreated infection but may appear as early as the first week or be delayed until the seventh or even the tenth week. In rare cases arthritis or other metastatic lesions are associated with gonococcal ophthalmia neonatorum or vulvo-vaginitis or may occur as a sign of relapse when sulphonamide treatment has failed

The joint manifestations of gonorrhœa may be classified —

Acute	*Sub-acute or Chronic.*
Diffuse arthralgia.	Hydrops articuli.
Acute arthritis (monarticular)	Osteo-arthritis.
Acute polyarthritis.	

Diffuse Arthralgia.—Pain is the prominent feature of diffuse gonococcal arthralgia, and tends to move about from joint to joint. No clinical signs may be apparent, except slight reddening and increased temperature of the skin over the affected joint(s) The history of shifting joint pains suggests acute articular rheumatism Gonococcal arthralgia however fails to respond to the administration of salicylates the temperature is seldom so high as in acute *rheumatism and the elicitation of symptoms and signs* of genital gonococcal infection should point to the correct diagnosis

Acute Arthritis.—The localisation of gonococcal inflammation to a single large joint commonly takes place during or after a stage of diffuse arthralgia. The joints involved in order of frequency are the knee ankle wrist shoulder hip and elbow The joint rapidly becomes swollen extremely tender to touch and active or passive movements are resisted because of pain The overlying skin is red and tense and there is a marked increase of local temperature The swelling is due to a sero-fibrinous exudate into the joint cavity the synovial membrane and the peri-synovial structures The tendons, ligaments and bursæ in relation to the affected joint are frequently involved while the muscles show marked and rapid wasting Frank suppuration is rare. Acute arthritis is accompanied by marked constitutional symptoms the temperature frequently varying between 100 and 103 F

Acute Polyarthritis.—Involvement of multiple small joints especially those of the hands and feet gives rise to acutely tender fusiform articular and peri-articular swellings, with cutaneous erythema and limitation of movement. Marked destruction of the ligaments may take place, leading to subsequent deformities may cause fibrous peri-articular thickenings or be followed by broadening and flattening of the joints. Constitutional disturbance is generally less than in acute monarticular arthritis.

Hydrops Articuli.—A sub-acute or chronic synovitis leading to hydrarthrosis is not infrequent especially during the sub-acute stages of a resolving gonococcal infection A single large joint, commonly the knee joint is involved and gradually becomes tense and swollen from serous exudate into the joint cavity The skin shows no erythematous changes, or rise in local temperature pain is absent or slight and movements of the joint are painless, but are limited mechanically by the effusion.

Osteo-Arthritis.—A sub-acute or chronic osteo-arthritis may occur involving a number of the smaller joints. There is a marked plastic sero-fibrinous exudate into the articular and peri-articular structures and erosion of the articular cartilage leading at first to pain and limitation of movement and later to deformity from cicatricial contracture

Diagnosis.—The occurrence of acute or sub-acute inflammatory changes involving one or more joints during the course of a genito-urinary gonorrhœa should suggest the probable cause Difficulty may be experienced in demonstrating the gonococcus when for example the urethral discharge in the male has temporarily become scanty or even absent when the arthritis occurs as a sign of relapse following the failure of sulphonamide therapy or when a history of gonococcal infection is denied. A

careful and if necessary repeated genito-urinary examination will reveal evidences of prostato-vesicular involvement in the male or involvement of the cervix and uterine adnexa in the female and will lead to the demonstration of the gonococcus The gonococcal complement fixation test is invariably positive and the application of this reaction in cases of acute rheumatism failing to react to the customary measures may point to the true aetiology

Treatment.—In every case in which metastatic complications of gonorrhoea have arisen treatment must be directed (1) to the eradication of the primary genito-urinary focus of infection and (2) to securing symptomatic relief and complete restoration of function of the affected joint or other structures. Gonococcal bursitis teno-synovitis, and arthritis are uninfluenced by the administration of the salicylates or other drugs of value in true rheumatic affections The sulphonamides are of undoubted value in many cases in clearing up the genito-urinary focus of infection but frequently fail completely to cure the metastatic lesions While the response to penicillin therapy in ordinary dosage has been satisfactory in cases of arthralgia and hydrarthrosis with minimal synovial changes even large doses of this drug (up to 3 000 000 Oxford units in five days) have failed to secure complete resolution in cases showing marked peri-articular involvement If a fever cabinet is available hyperpyrexial therapy is the treatment of choice in dealing with gonococcal infections of joints muscles ligaments, etc. Dramatic symptomatic relief and clinical improvement follow a fever session of eight hours at a temperature of 106 to 106·7 F complete recovery may however necessitate three or five pyrexias Subsequent surveillance is necessary to make certain of cure of the genito-urinary infection while massage graduated exercises or other remedial measures may be indicated to

obtain full functional recovery of the structures involved in the metastatic lesion. If hyperpyrexial treatment is not available sulphonamide or penicillin administration should be reinforced by a series of fevers induced on alternate days or every third day according to the condition of the patient by the intravenous injection of T.A.B vaccine, pyrifer or *B coli* vaccine Improvement is less rapid than with physical hyperpyrexia and the joint should be rested by means of a suitable splint or bi valved plaster of Paris case to promote the relief of pain and prevent the development of subluxation or other orthopaedic deformity

Myositis.—Myalgia or acute or sub-acute myositis may occur at any time during the course of gonococcal infection. While the muscles most commonly involved are those in relation to an infected joint cases not infrequently occur of affection of muscles especially those of the back without concomitant arthritis. Fleeting myalgic pains without apparent anatomical changes occur worse on rising in the morning, and associated with some muscular stiffness. The symptoms gradually improve during the day In acute or sub-acute myositis pain of varying severity is constant movement of the affected muscles is limited and on examination localised or diffuse areas of tenderness are detected with or without palpable inflammatory swellings in the course of the muscle. Atrophy of the affected muscle is rapid.

Periostitis and Osteitis.—Involvement of the periosteum bone or bone marrow usually occurs in association with a gonococcal tenosynovitis or arthritis but may arise as a solitary metastatic lesion. The calcaneus, the tibia, and the distal extremity of the ulna are the bones most frequently involved. Localised periostitis leads to the formation of exostoses the common site being the tubercle of the os calcis. In this situation exostoses are bilateral or infrequently unilateral and give rise to a painful heel (gono-

coccal heel (sub-calcanean spur). Tenderness on standing or on pressure over the centre of the ball of the heel is suggestive, and the X-ray appearances are characteristic. Diffuse periostitis gives rise to irregular bony thickenings. Osteitis or osteomyelitis is rare, the symptoms being

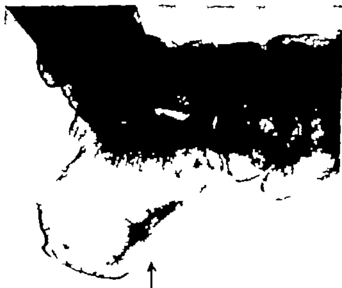


FIG. 48.
X-ray: sub-calcanean spur.

similar to those of osteomyelitis occurring in other bacterial infections.

The principles of diagnosis and treatment are as for arthritis.

Endocarditis, Myocarditis, Pericarditis.—An insidious verrucose or ulcerative endocarditis involving the mitral or aortic valves may occur during the course of blood

stream gonococcal infection commonly in association with acute arthritis or tenosynovitis. The gonococcus is demonstrable in the blood stream during life and in the diseased heart valves after death. The symptoms, signs and clinical course are indistinguishable from those of an acute rheumatic endocarditis. The occurrence during an attack of gonorrhœa of symptoms referable to the cardiovascular system must therefore be viewed with concern. Myocarditis is rarely recognised, although it seems not improbable that transient toxic myocarditis must occur not infrequently in systemic gonococcal infection. The symptoms of the more serious types are those of infective myocarditis with well marked and rapidly progressive cardiac dilatation. Pericarditis is rare and invariably occurs *in association with endocarditis or myocarditis*

Pleurisy Peritonitis, Meningitis.—Blood-stream dissemination of the gonococcus may lead to infection of the pleural or peritoneal sacs or rarely of the meninges the resulting clinical picture being that of similar conditions of other bacterial ætiology The occurrence of a pleurisy or a peritonitis in association with gonorrhœa suggests the cause absolute proof is only obtainable by demonstration of the gonococcus in the inflammatory exudate

Neuroses.—During the course of treatment of gonorrhœa a number of patients, most commonly males, become mentally depressed morbidly introspective despondent of cure fix their minds firmly on their uro-genital apparatuses and magnify any trivial symptoms or signs to the most serious magnitude. Constipation, neuralgic pains dyspepsia, prostatorrhœa nocturnal emissions impotence or discomfort referred to the urethra or perineum are the presenting symptoms. Phosphaturia oxaluria or uraturia are frequently present A thorough clinical examination at the onset of the disease and careful subsequent treat

ment will inspire the patient with confidence and go far to prevent the development of psychosis. The patient's queries should be answered fully and patiently and the necessity for prolonged observation after apparent cure fully explained. The attitude of the clinician should be optimistic.

When the neurosis has persisted for some time before the patient is examined it is of the utmost importance to make certain that there is no residual lesion in the genito-urinary tract which may act as a physical basis in the causation of symptoms In the absence of such findings local treatment must be resolutely withheld and the patient referred to a psychologist if the assurance of the clinician is not followed by a change of mental attitude

Neuritis and Neuralgias.—Minor degrees of neuritis and neuralgia may occur during the course of a gonococcal infection They present no special characteristics and generally disappear as the gonorrhoea improves. A chronic sciatic pain is frequently associated with a sub-acute or chronic prostato-vesiculitis of gonococcal or non-gonococcal origin.

MUCO-CUTANEOUS MANIFESTATIONS OF GONORRHŒA

The muco-cutaneous manifestations of gonorrhœa are rare They can be classified —

(1) Localised abscesses or ulcers.
(2) Erythemata of scarlatiniform or morbilliform type.
(3) Urticarial rashes erythema nodosum erythema multiforme
(4) Keratoderma blenorrhagica.
(5) Gonococcal stomatitis and rhinitis

Localised Abscesses may occur on the genitalia, especially on the raphe of the penis from gonococcal infection of the sebaceous ducts or from suppuration in the lymphatic

vessels. *Ulcers* may subsequently form. The gonococcus is the sole organism demonstrable in these abscesses or ulcers.

Erythematous Eruptions.—A generalised scarlatiniform, morbilliform or less frequently erythema multiforme-like eruption may occur in cases of acute gonorrhœa. In more severe cases, especially where there is blood-stream infection the rash may become purpuric. These erythemata must be distinguished from *secondary syphilides* and *drug rashes*, *e g* following copaiba or sulphonamide therapy



Fig 49.
Keratoderma blenorrhagica, showing pustular stage and early keratinisation

Urticaria and Erythema Nodosum of gonococcal aetiology are indistinguishable from similar conditions of other causation. Their occurrence however in association with metastatic lesions of gonorrhœa especially arthritis suggests the possible cause.

Keratoderma Blenorrhagica (gonococcal hyperkeratosis) is the most characteristic although rare eruption occurring during the course of a gonococcal infection It is almost entirely confined to males, and is invariably associated with arthritis and toxic conjunctivitis. The sites commonly involved are the soles the toes the dorsa of the

feet the legs the penis the scalp and the nails of the toes or fingers. The condition commences about the fourth or fifth week of gonococcal infection as a vesicular eruption which rapidly passes into a pustular stage. Keratinisation takes place in the wall of the pustule the core becomes dried up and waxy and is composed chiefly of leucocytes and epithelial cells forming a raised papule with a horny centre and a tendency to crusting Proliferation of the cornified centre of the lesion gives rise to a characteristic raised limpet-shell-like lesion, aptly likened to mountains on a relief map The hyperkeratotic papules may remain discrete or may coalesce giving rise to plaques of varying size



Fig 50
Keratoderma blenorrhagica, showing typical limpet-shell-like crusts

Keratoderma blenorrhagica must be differentiated from crustaceous frambœsiform and rupial syphilides while the discrete lesions on the trunk may closely resemble rupioid psoriasis. The pyrexia and severe cachexia accompanying gonococcal hyperkeratosis the genital infection arthritis and toxic conjunctivitis or iritis should make the differential diagnosis easy Gonococci cannot invariably be demonstrated in the secretions a similar syndrome—keratoderma associated with pyrexia cachexia arthritis and conjunctivitis or iritis—was described in association with non-gonococcal urethritis by Reiter in 1916 More recent observations have shown that the skin lesions in Reiter disease and gonococcal hyperkeratosis are identical and

that the cause is most probably a virus, infection with which may be concomitant with gonorrhœa. The course of keratoderma is cut short by the application of pyrexial measures to the associated arthritis. The local lesions require no treatment apart from some emollient application.

Gonococcal Stomatitis and Rhinitis.—Involvement of the buccal and nasal mucous membranes is exceptionally rare. In the new-born infant direct infection may occur from infective maternal secretion during the process of birth, or later in association with ophthalmia neonatorum by the passage of gonococci through the lachrymal ducts. In adults infection is digitally transferred from the genital focus or may result from perversions. An acute localised or generalised inflammatory stomatitis or rhinitis follows with increase of the secretions and frequently the formation of greyish or greyish-green membrane. In the investigation of such cases the gonococcus must be carefully differentiated from the other organisms of the Neisserian group which more commonly occur in the nose or mouth.

CHAPTER XVIII

VULVO-VAGINITIS

THE term vulvo-vaginitis includes a number of prepubertal infections which may vary greatly in bacterial aetiology symptoms and clinical signs. Epidemics may occur amongst children in institutions.

Modes of Infection.—*Direct infection* may occur from criminal assault precocious sexual intercourse or perversions or infrequently in utero or during the process of birth. *Indirect means* are the usual modes of conveying infection—infected bedclothes, towels nurses aprons chamber pots lavatory seats bath water and rectal thermometers have all been incriminated.

Vulvo-Vaginitis may be classified as —

(1) *Gonococcal* (highly contagious—approximately 10 to 15 per cent of all cases)

(2) *Non-gonococcal* (low contagiousness) —

( ) *Bacterial* (direct local infection)	(b) *Protozoal*	( ) *I [illegible]* —
Enterococci Coliform bacilli Staphylococci Pneumococci B Diphtheriae (Infection carried digitally from faecal or nasal infection or from rectum)	Trichomona vaginalis infestation (rare)	Systemic disease— Chicken pox Scarlatina Other exanthemata, Coryza, Pneumonia, etc

Certain factors predispose to or cause localisation of infection *e g* a chronic local uncleanliness irritation from dirty clothing, inadequate clothing permitting easy contact with infective material chronic masturbation foreign

bodies in the vagina or thread worm infestation of the bowel.

The Vagina in Infancy.—Before puberty infection in the child is almost invariably limited to the vulva vagina and urethra. At birth the vagina is covered with thick stratified squamous epithelium much glycogen being present. The secretion is highly acid often profuse and may be confused with an infective condition. There are however no accompanying inflammatory changes. This adult type of vaginal mucosa is due to œstrin absorbed from the maternal circulation. In the course of from one to three months the œstrin disappears from the infant's circulation and the mucosa becomes thin and composed of cubical cells, devoid of glycogen. The secretion is by now scanty and alkaline. It remains in this state until puberty when the adult development of the genitalia and mucous membrane occurs. The non-involvement of the cervix and of the Bartholinian glands in prepubertal infection must be attributed to the functional under-development of these organs.

Symptoms and Signs.—The symptoms and signs may be trivial or very severe. Dysuria, increased frequency of micturition and local irritation are present in varying degree. Occasionally there may be retention of urine or acute or sub-acute lower abdominal pain which may be confused with appendicitis. On examination mild or severe vulval inflammation or redness is observed with frequently some generalised œdema. The inflammatory changes may extend down the inner aspect of the thighs. A slight or profuse vaginal discharge is present. The urethra is involved in 80 to 90 per cent of cases. A scanty serous discharge is usual less commonly this is profuse and muco-purulent or purulent. In the chronic carrier cases the clinical findings are often minimal or intermittent. There is the danger that such cases may

be missed and an epidemic spread caused *e.g* in an institution or ward for children unless the strictest nursing precautions are observed.

Diagnosis.—It is of the utmost importance to establish whether any given case of vulvo-vaginitis is due to the gonococcus or not. Failure to make a correct diagnosis may be due to casual examination to inexpert collection of material for bacteriological examination or to attempting examination of the child with inadequate assistance. The child must be examined in the lithotomy position with the thighs separated as far as possible. A good light is essential. Any superficial discharge is removed by moist swabbing the vulva is inspected and the labia separated by the gloved forefinger and thumb of the left hand. Any discharge lying external to the vaginal introitus must be carefully mopped away Specimens for bacteriological examination—slides or cultures—must be taken, either with a wire loop or with sterile swabs, from the interior of the vagina and urethra If there is any discharge or suspicious redness swabs should be taken from the rectum. Rectal swabbing should never be omitted in relapsing cases The complement fixation test is usually negative in the early stages of gonococcal vulvo-vaginitis and is therefore of little value in early diagnosis. Opinions as to its value in the later stages of vulvo-vaginitis are conflicting The test may remain negative throughout the course of the infection if on the other hand it has become positive during the earlier stages then it is of value in tests of cure

Complications.—*Proctitis* results from direct spread of infection and occurs in from 10 to 15 per cent of cases. The symptoms are rectal irritation and less commonly tenesmus or pain on defecation Peri anal redness and slight œdema are noted on examination while there may be superficial excoriations or deeper ulcerations from

scratching. Rectal infection may be asymptomatic. *Cervicitis* occurs in from 2 to 5 per cent. of cases. While it is unnecessary to examine the cervix as a routine, it is essential that it should be investigated and if necessary treated in relapsing cases. The technique is similar to that in the adult, using suitably small instruments. A distal lighting short endoscopic cannula gives adequate exposure and satisfactory illumination; alternatively a Ferguson type speculum or a Dawson's urethral speculum may be employed. Extension of infection to the *endometrium*, *Fallopian tubes* or *pelvic peritoneum* rarely occurs. *Cystitis* is also rare despite the frequency of infection of the urethra.

Treatment.—Treatment may be considered under the following headings:—

(1) General treatment.
(2) Local Treatment.
(3) Penicillin, sulphonamides, oestrin, vaccines, pyrexia.

General Treatment.—The application of penicillin and the sulphonamide group of drugs have greatly diminished the relative importance of local treatment and other ancillary measures. Hospitalisation is advisable but is by no means essential for acute infections. The diet should be light but adequate and balanced. Milk, fruit and fresh vegetables are essential; the carbohydrate intake should not be excessive. Special attention should be devoted to combating anaemia or nutritional defects according to general medical principles.

Penicillin has proved an effective agent in the treatment of gonococcal vulvo-vaginitis; the general scheme of administration and the dosage are the same as for gonorrhoea in the adult. Symptomatic relief is rapid and after twenty-four hours no abnormal clinical signs are found. At this stage urethral and vaginal smears m

show the presence of a small number of pus cells gonococci are however absent and the smears become pus-free in a further twenty four to seventy two hours. Further courses of penicillin are indicated by the persistence twenty four hours after treatment of local signs of inflammation or of much pus in the smears.

While no failures have been noted so far it seems not improbable that a certain percentage of cases will fail to be cured by penicillin and the most careful surveillance must be advised.

Sulphonamide Therapy—Sulphapyridine sulphathiazole and sulphadiazine are equally efficacious in causing rapid symptomatic relief and in permanently curing a large percentage of cases The dosage is dependent upon the age and general condition of the patient an approximate guide for younger children being —

Age	*Dosage* (I tablets [illegible] hourly)	*Total gm per 24 hour*
Under 6 months	[illegible] or [illegible] alternating with [illegible]	75 5 gm
6 months to years	[illegible] or [illegible] alternating with [illegible]	5 8 gm
t 4 years	[illegible]	5 gm
5 to 6 years		3 gm

This dosage is continued for five days and has not been followed by other than occasional intolerance.

Local Treatment—If the discharge is profuse a mildly antiseptic or alkaline sitz bath given immediately before examination facilitates the cleansing of the vulva. The vagina and urethra may be treated by irrigation or by moist swabbing and subsequent topical application of antiseptics. The following solutions have been advocated

for vaginal douching ½ per cent. protargol weak tincture of iodine ʒi to one pint potassium permanganate 1/5 000 chloramine-T 1/5000 The chosen lotion is applied through a small-bore rubber catheter attached to a douche can The temperature of the lotion should be 90 to 100 F and the can should not be raised more than one foot above the level of the pelvis. For the urethra, potassium permanganate is the most useful irrigant As an alternative to wet treatment the gross accumulation of inflammatory products is removed by moist swabbing and the vagina and urethra carefully painted with ½ per cent. aqueous solution of picric acid 4 per cent. mercurochrome or 10 per cent. protargol in glycerine. Local treatment should be carried out daily during the stage of profuse discharge and with gradually lessening frequency as the condition improves. *Proctitis* yields rapidly to daily douching with 1/5 000 potassium permanganate and subsequent insertion of protargol suppositories. The sulphonamides are by no means invariably successful. The local treatment of *cervical infection* must be carried out by direct vision and on lines similar to those advised for the adult female.

Oestrin Treatment.—The rationale of oestrin treatment is to substitute for the infantile vaginal mucosa the stratified adult type which is refractory to the gonococcus. If therefore the infection is localised to the vagina, eradication is possible. Oestrin should be given by injection in daily dosage of 3 000 to 6 000 units according to the age and weight of the child Alternatively vaginal suppositories (500 to 1000 units) may be employed. The duration of treatment varies from a few weeks to a few months It is essential before therapeutically applying oestrin that the urethra and the rectum are free from infection Certain sequelæ may occur engorgement of the breasts, vaginal hæmorrhage and masturbation

Vaccines.—Prior to the introduction of penicillin and the sulphonamides vaccines proved a useful adjuvant to treatment now these are indicated only in the case of failure of these remedies. A reliable stock or autogenous detoxicated gonococcal vaccine should be employed. Children tolerate relatively greater doses of vaccine than adults according to the age and weight of the child the commencing dose should be one-quarter to one-tenth of that recommended for the adult subsequent injections being regulated according to the local and systemic reaction

Hyperpyrexial Treatment.—The methods applicable to vulvo-vaginitis are as described under neuro-syphilis. The best results follow physical hyperpyrexia a series of treatments of eight hours at 106 F being given.

Treatment of Relapses.—In view of the great liability of gonococcal vulvo-vaginitis to relapse prolonged clinical observation and repeated bacteriological tests must be carried out before definite cure can be assumed Relapse may be indicated by the recurrence of frank signs and symptoms More commonly however the signs of relapse are trivial and often intermittent. A slight vulval redness and moistness or an intermittent frequently scanty mucoid vaginal discharge should indicate the necessity for searching bacteriological examination In these cases special attention should be paid in the physical examination to the possibility of cervical or rectal infection. Treatment of relapse cases should be first by a combination of local therapy and vaccine administration followed by a further course of penicillin or sulphonamides. If this fails œstrin or hyperprexia should be considered.

It is important to exclude any possible familial sources of reinfection which may account for otherwise inexplicable relapses."

Criteria of Cure.—After the disappearance of signs and symptoms the child should be kept under observation for a

minimum period of six months. Clinical examination and smears or cultures should be carried out weekly for the first eight weeks and thereafter at fortnightly or monthly intervals. The complement fixation test, if positive during the course of infection should revert to negative during the surveillance period. Consistently negative findings are necessary to establish a cure.

Preventive Aspects.—In dealing with a case of vulvo-vaginitis every effort must be made to prevent the infection of other children. Similarly all children who have been in contact with a known case should be carefully examined, clinically and bacteriologically. Prophylactic application of a colloidal silver preparation or a full course of penicillin or of sulphonamides may be considered according to the urgency of the situation but this must be followed by an observation period of at least three months. A routine inspection should invariably be made of all admissions to children's institutions or wards and any patient showing suspicious signs isolated until a diagnosis is reached. The strictest nursing precautions should be maintained to prevent any possible transfer of infection.

Non-gonococcal Vulvo-Vaginitis.—Attention must be directed to the elimination of any systemic causal factors. The milder cases often respond to simple local cleanliness. The more severe types are treated by local measures similar to those for gonococcal cases. Oestrin therapy is frequently of value.

CHAPTER XIX

GONOCOCCAL INFECTIONS OF THE EYE

THE eye may be involved at any time during the course of a gonococcal infection by transfer of infective material from the genito-urinary focus, or metastatically as a systemic complication. In the newborn child infection of the conjunctival sac (*ophthalmia neonatorum*) results from direct inoculation during the process of birth. The various manifestations are:—

Resulting from Direct Inoculation	*Resulting from Metastatic Infection*
Ophthalmia Neonatorum	Toxic Conjunctivitis
Purulent Gonococcal Conjunctivitis (after the third week of life)	Iritis.

Ophthalmia Neonatorum is defined as "any inflammation of the eyes of an infant accompanied by a purulent discharge from the eyes commencing within twenty-one days from the date of birth." Ophthalmia neonatorum is notifiable to the Medical Officer of Health of the Maternity and Child Welfare Authority for the district. The penalty for failing to notify a case is a fine not exceeding £100, *with a penalty of £50 per diem for a continuing offence.*

Effect of Pregnancy and Labour on Gonococcal Infections.—Recently acquired gonococcal infections may pursue an unpredictable course during pregnancy. In many cases the disease is apparently trivial with few symptoms or signs; in others it is of the utmost severity. An old gonococcal infection may remain latent and lead to conjunctivitis in successive children or labour may cause reactivation and liability to adnexal inflammation or puerperal sepsis.

Bacteriological Aetiology.—Ophthalmia neonatorum

may be due to the gonococcus or to other organisms. In the past the gonococcus was responsible for approximately two-thirds of all cases. In recent years however the percentage of cases caused by the gonococcus has fallen to twenty five or less. Other organisms frequently associated with this condition are the pneumococcus B coli Koch-Weeks bacillus Morax Axenfeld bacillus, Friedländer s pneumobacillus Pfeiffer s influenza bacillus bacillus pyocyaneus micrococcus catarrhalis and in rare cases the diphtheria bacillus. The most potentially serious cases, i.e. those in which sight is most likely to be imperilled are those caused by the gonococcus.

Time and Mechanism of Infection of the Eyes.—Infection of the conjunctival sac most frequently occurs immediately after delivery and opening of the infant's eyes from infective maternal secretion deposited on the eyelids during parturition. Intra-uterine infection is rare. Intra partum infection may occur in vertex presentations the child normally passes through the vagina with the eyelids tightly closed and slightly inverted. In protracted labour infection may be caused by pressure of the perineal band forcing infective material between the eyelids. Post partum infection may be conveyed by the hands or fingers of the infant or accoucheur towels, etc

Incubation Period.—In gonococcal infections the incubation period is usually short inflammatory signs being present by the third or fourth day In cases due to other organisms the incubation period may be short but generally varies from seven to twenty days. The longer the incubation period the more likelihood there is of a mild infection with little risk of corneal damage

Clinical Course.—The earliest sign to be detected is a transverse reddening of the conjunctiva of the upper eyelid. This is rapidly followed by generalised injection and tumefaction and a thin serous or sero-purulent

discharge As the condition progresses the eyelids become red swollen hot and glazed there is a profuse purulent often sanious discharge from the conjunctival sac. Œdema of the upper lid may be so extensive as to cause it markedly to overlap the lower and renders inspection of the cornea difficult In the absence of treatment the cornea [illegible] a ground-glass appearance and ulceration occurs, l[illegible] to macula nebula, or leucoma formation Chemosis may lead to marginal ulceration of the cornea. In fulminating cases the cornea may perforate in twenty four to thirty six hours with escape of the aqueous and prolapse of the iris Impairment or complete loss of sight may result from leucoma, panophthalmitis or secondary glaucoma.

Complications.—While local and systemic complications of ophthalmia neonatorum are rare they are liable to occur and a careful watch must be kept to detect them at the earliest possible moment. A tender inflammatory adenitis of the pre-auricular gland which seldom suppurates is not infrequent Abscess formation in the eyelids cellulitis of the orbit infection of the ethmoid air cells and meningitis may occur but are seldom met with. Infection of the lachrymal duct may lead to gonococcal rhinitis in cases showing no other complications Stomatitis or vulvo-vaginitis may occur in association with ophthalmia neonatorum any of the metastatic complications more commonly the sequel of genital gonorrhœa, may occur in ophthalmia neonatorum of these the least infrequent is arthritis

Diagnosis.— In every case of conjunctival inflammation occurring in a child shortly after birth the diagnosis of ophthalmia neonatorum is clinically obvious. The only condition which may be confused is the conjunctival redness and mu[illegible]id or slight muco-purulent secretion which may follow pr[illegible]phylactic instillation of silver nitrate or less frequently ot[illegible]r [illegible]ilver salts In cases due to gonococcal or

her bacterial infection the causal organism is easily emonstrable microscopically Cultures and fermentation eactions are however necessary to differentiate between he various organisms of the Neisseria group which may be etiological factors in ophthalmia neonatorum. In catarrhal conjunctivitis following prophylaxis smears show much mucus admixed with pus cells, and an entire absence of organisms while there is no growth on culture.

Prognosis.—The potential seriousness of ophthalmia neonatorum has been greatly decreased by early diagnosis and prompt treatment. The earlier treatment is undertaken the less risk there is of subsequent corneal damage. The various factors affecting the prognosis are the stage of the disease and condition of the cornea, the bacterial cause the size of the palpebral fissure, and the nutrition of the child.

Treatment.—The application of the sulphonamides or penicillin has revolutionised the treatment of ophthalmia neonatorum and has decreased the length of treatment from weeks to hours.

Penicillin in dosage of 150 000 to 200 000 Oxford units in twelve hours, cures dramatically Alternatively the local application of drops containing 1000 to 2000 Oxford units per c.c. may be employed

Sulphonamide Therapy.—Sulphapyridine sulphathiazole or sulphadiazine are equally efficacious. The commencing dose is ¼ tablet (one-eighth gm.) four hourly for 24 hours. If no intolerance follows this therapy the dose is increased to ½ tablet alternating with ¼ tablet at the same intervals and continued for three to four days according to the progress.

Local Treatment.—If the condition is unilateral the unaffected eye must be protected by a Buller's shield. The conjunctival sac should be kept pus-free by frequent lavage with weak antiseptics, *e.g.* boric lotion, normal

saline or 1/20 000 potassium permanganate Lavage should be at intervals of from one-half to two hours during the early stages the time interval being gradually extended as improvement occurs. In those cases, infrequently met with *which fail to react to sulphonamides*, local treatment should be persevered with in addition 1 per cent atropine drops should be instilled into the eye once daily and 1/1 500 flavine in castor oil four hourly The administration of a polyvalent detoxicated vaccine (initial dose 1/100 c c. equivalent to 500 million organisms) should be commenced without delay and a further course of sulphonamide given in from ten to fourteen days.

Preventive Aspects.—The surest method of preventing the occurrence of ophthalmia neonatorum is by the early diagnosis adequate treatment and high standard of tests of cure of gonorrhoea in the male and female In this connection also it is important to investigate all vaginal discharges occurring in pregnant women the application of the appropriate treatment is of value in reducing the incidence of non-gonococcal ophthalmia neonatorum. Latent infection may not infrequently occur in males or females and in only approximately 70 per cent. of the mothers of children developing ophthalmia neonatorum can a history of vaginal discharge during pregnancy be elicited The occurrence of ophthalmia neonatorum in an infant should be followed by the investigation of the mother

Prophylactic Measures Applied to the Child.—Prophylaxis is only of value in cases of intra partum or immediate post partum infection where the organisms are lying free in the conjunctival sac and are freely accessible to the antiseptics Prophylaxis is of no value in cases in which inflammatory changes of the eyes are present at birth and equally does not prevent post partum infection Prophylaxis must be combined with certain supple-

mentary nursing measures if it is to be effective. The child's eyelids should be cleansed with some mild antiseptic and all adherent matter removed as soon as possible after the head is born and before the child has had time to open the eyes. As soon after birth as is possible the lids are gently separated by an assistant and with a glass rod a single drop of 1 per cent. silver nitrate is placed in the outer canthus of each eye. After approximately one minute the eyes are flushed out with normal saline solution. Nursing precautions are directed towards prevention of conveyance of infected secretion to the baby's eyes by the infant's or attendants' hands or by towels etc.

In a certain percentage of cases the prophylactic application of silver nitrate may be followed by a mild or more severe conjunctival catarrh. This may be mistaken for the onset of an ophthalmia neonatorum; immediate bacteriological examination of the conjunctival secretion will aid in the differential diagnosis. In the absence of demonstration of gonococci the catarrh will settle down in twenty-four or thirty-six hours with simple saline irrigation. The occurrence of conjunctival catarrh following silver nitrate prophylaxis has led to the trial of many other drugs. Other silver salts which have been used successfully are protargol, argyrol, lunosol, or neoprotosil. These cause no reaction in strengths of up to 10 per cent. but to be effective must be used in freshly prepared solution.

Purulent Gonococcal Conjunctivitis.—Infection of the conjunctival sac may take place at any time in life subsequent to the period during which ophthalmia neonatorum occurs. The eyes are usually infected by the digital conveyance of infective secretion from a genital gonorrhœa or through the medium of towels, sponges, or other soiled toilet articles. The latter mechanism also accounts for the

sporadic cases of gonococcal ophthalmia infrequently met with *i.e. when the eye is involved without concomitant* genital infection

The incubation period and clinical course are similar to those of ophthalmia neonatorum but are frequently more *rapid and severe In the early stages* bacteriological examination differentiates the condition from a toxic conjunctivitis occurring in the course of a gonorrhœa, or



F 5
End result in gonococcal ophthalmia showing dense leucoma and total loss of vision in left eye

from a conjunctivitis due to other bacterial causes in the more advanced cases the clinical picture is unmistakable Treatment is essentially similar to that for ophthalmia neonatorum

Toxic Conjunctivitis.—A metastatic or toxic conjunctivitis may occur in adults as an accompaniment of gonorrhœa with other complications such as arthritis. The conjunctiva is red and œdematous photophobia is marked and there is a scanty mucoid or muco-purulent discharge sufficient to cause glueing together of the eyelids. Bacteriological examination reveals that the exudate is composed of muco-pus with an entire absence of the gonococcus or other organisms. Toxic conjunctivitis

recovers as improvement occurs in the primary genito-urinary lesion Photophobia necessitates the wearing of an eye shade no other local treatment is usually indicated In severe cases however the intravenous injection of calcium salts is of value in procuring temporary symptomatic relief.

Gonococcal Iritis.—This metastatic condition which attacks adult males exclusively is commonly associated with prostato-vesiculitis or with arthritis of the larger joints. The affection is usually unilateral the course is chronic, and liability to relapse is marked The earliest sign of iritis is the occurrence of a zone of pink discoloration round the margin of the cornea from dilatation and congestion of the episcleral branches of the anterior ciliary arteries. The injection is most marked at the margin of the cornea and may be associated with conjunctival congestion. During the attack the patient experiences neuralgic pains in the eyeball and head. Photophobia and lacrymation occur in varying degree Disturbance of vision may be the earliest symptom and results from haziness of the media from exudate or spasm of accommodation. The characteristic signs of iritis are loss of pupillary reaction to light and to mydriatics loss of lustre and frequently a greenish alteration of colour of the surface of the iris and the occurrence of exudate in the anterior chamber Adhesions are uncommon in gonococcal iritis

Diagnosis—In the early stages iritis may be mistaken for conjunctivitis In the latter however there is no discoloration of the iris the pupil reacts promptly neuralgic pain is absent and muco-purulent secretion is present leading to gumming of the eyelids. The instillation of atropine results in prompt and regular dilatation of the pupil If no adhesions are present the diagnosis of iritis depends on the presence of peri-corneal injection sluggish pupil reaction to light and discoloration of the iris. The

iritis associated with early generalised syphilis is usually bilateral, and there is a great tendency to exudation of lymph (plastic iritis) the formation of posterior synechiæ and the occurrence of lymph nodules on the iris.

Treatment —While recovery from an attack of gonococcal iritis depends upon the eradication of the causal genito-urinary focus local treatment is of value in affording symptomatic relief in preventing the formation of adhesions of the iris and in promoting absorption of the inflammatory exudate. Severe photophobia necessitates rest in a *darkened room in milder cases the provision of smoked* glasses is essential Relief of pain and neuralgia follows the dilatation of the pupil by atropine and the application of local heat. Full dilatation of the pupil should be achieved by instillation of 1 per cent atropine drops and maintained for a week or ten days after the disappearance of all symptoms The local application of heat is by fomentations an electrically heated pad or diathermy In cases in which *hyperpyrexia is indicated for other complications of gonorrhœa, this measure cuts short the* attack of iritis relapse may however follow

The outlook in cases of gonococcal iritis is variable a large number of cases recover completely and suffer no recurrence *In other instances there is chronic liability to* relapse In these cases the use of vaccines is of undoubted benefit.

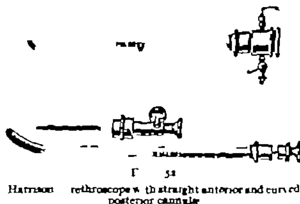
CHAPTER XX

URETHROSCOPY

IN the investigation of persistent infections of the male or female urethra visual inspection of the urethral mucous membrane and its glandular openings (urethroscopy) affords accurate information as to the state of these structures which often cannot otherwise be gained and which leads to the application of the most efficacious treatment. The urethroscope is also of great value in the investigation of endocervicitis complicating vulvo-vaginitis in immature girls, in the tests of cure of gonorrhœa in the adult and to a less extent for intra-urethral operative procedures in the male or female.

The urethroscope consists essentially of (1) a cannula flanged at the external end and having a well-fitting obturator to facilitate introduction (2) lighting and magnifying visual systems which are usually combined, and are attached to the flange after the cannula is in position and the obturator withdrawn and (3) an attachment to permit distension of the urethra by air or water pressure. The lighting system may be external or internal. In the former the source of light is outside the endoscopic tube the visual field being illuminated by a pencil of light reflected by a mirror or prism in the latter type a miniature electric bulb mounted on a slender stem is positioned in the assembled instrument near the internal opening of the urethroscopic tube. For urethroscopy of the anterior urethra an air-distension internal-illumination instrument such as Harrison's urethroscope is employed with straight cannulæ of varying size to suit the calibre of the individual urethra. For posterior urethroscopy the same instrument

may be used with special cannulæ curved near the tip and having a window at the convexity of the beak. Special water-distension urethroscopes such as the Geringer are however preferable and give a better view of the structures in the membranous or prostatic urethra. Urethroscopy is practically painless if the examination is expertly carried out if a cannula size suitable for the calibre of the urethra



F 52

Harrison rethroscope with straight anterior and curved posterior cannulæ

is chosen and if care is taken to avoid too great or prolonged distension of the urethral canal. In anterior urethroscopy the use of local anæsthesia should where possible be avoided because of the alteration caused in the appearance of the mucous membrane in posterior urethroscopy local analgesia is essential despite the mucosal anæmia caused.

Indications for Use of the Urethroscope.—These can be summarised as —

(1) In the investigation of sub-acute and chronic urethritis in male or female failing to resolve under the accustomed measures.

(2) In th final tests of cure of gonorrhœa, to make

certain of restitution to normal of the urethral structures.

(3) To investigate and obtain serum for dark-ground examination in cases of suspected intra urethral chancre.

(4) For local treatment of intra-urethral warts polypi, etc. For trans-urethral incision of peri-urethral abscesses. (Urethroscopic treatment by probe or cautery for chronic infection of Littré s glands is seldom advisable.)

(5) In the investigation and treatment of the endocervix in refractory cases of vulvo-vaginitis.

Urethroscopy is in general *contra-indicated* by the presence of acute (or an acute exacerbation of) urethritis and by the presence of acute local complications. The patient should have only a scanty mucoid, or muco-purulent urethral discharge, and the urine should be clear although showing a flocculate of threads.

Technique of Anterior Urethroscopy—Except in cases such as the urethroscopic incision of a peri-urethral abscess when the bladder should be emptied and antiseptic urethral irrigation carried out before instrumentation the patient for urethroscopy should not have micturated for at least three to four hours prior to examination and no preliminary urethral lavage should be given The strictest rules of antisepsis should be observed and the greatest care taken in the sterilisation of the instrument the lubricant the operator s hands, and the glans penis. The patient may lie flat on an examination couch with the pelvis slightly raised on a firm flat cushion or is placed in the lithotomy position with the legs and feet resting comfortably on supports. In the former case the operator stands on the right of the patient in the latter he sits between the patient s thighs.

The urethroscopic tube with its obturator in position is lubricated and introduced into the urethra the tip being directed towards and reaching the junction of the b r

and membranous urethræ. The obturator is withdrawn and any excess of lubricant is gently mopped out by passing probe-sticks dressed with cotton wool down the cannula. If any free bleeding caused by the introduction of the cannula is not immediately controlled by gentle pressure with the dressed probe it is wise to withdraw the cannula and defer examination to a later date because of the possible risk of embolism when using air pressure to distend the urethra and the difficulty of obtaining a clear field After removing the excess of moisture the lighting and visual systems are attached to the cannula and as the instrument is slowly withdrawn each successive field from the bulb to the external meatus is carefully studied The cannula should be directed so that its lumen lies in the long axis of the urethra and the tip centred on the immediately proximal undistended portion of the urethra. In cases of difficulty slight air distension is of great assistance in the correct centring of the instrument.

On looking down a urethroscope when no air dilatation has been applied the image is seen to consist of two parts, a central figure and the mucous surface Normally the walls of the urethra are in apposition the mucous membrane being thrown into longitudinal folds The passage of the urethroscopic tube forces the walls apart a short distance beyond the tip of the cannula the walls close together giving rise in effect to a shallow funnel of mucous membrane converging proximally from the internal end of the endoscopic tube into the potential lumen of the urethra. The neck of this funnel *i.e* the potential lumen of the collapsed urethra forms the central figure The mucous surface is formed by the urethral mucous membrane separating to surround the cannula. This gives a wheel-spoke appearance due to the radiation of the longitudinal folds of the urethra from the central figure to the periphery

As the various portions of the urethra are in turn examined during the course of a urethroscopy careful observation should be made of —

(1) The form of the central figure

(2) The colour and appearance of the mucous membrane, and the regularity of the radial striations

(3) The appearance of the openings of Littré's gland ducts and of the lacunæ of Morgagni.

(4) The ease of dilatability of the urethra under air distension and the subsequent contractility when the air pressure is discontinued.

The application of air pressure causes ballooning of the urethra and besides permitting assessment of its resiliency greatly widens the field of view and stretches the openings of the Littré's gland ducts and lacunæ of Morgagni making these structures more prominent

Urethroscopic Appearances of Normal Anterior Urethra. —The mucous membrane of the healthy urethra shows considerable variation in colour not only in different individuals but also in different portions of the same urethra. The colour progressively deepens proximally from an anæmic yellow or yellowish-pink in the region of the glans penis to a full red transfused with yellow in the bulb The colour is dependent upon the frequency of the blood vessels, which running longitudinally in the submucous tissues impart to the mucosa its characteristic hue and vascular striations The smooth epithelial surface of the urethra lubricated by the alkaline secretion of the Littré's glands has a characteristic lustre

In the *bulbous urethra* the central figure is a transverse slit the longitudinal folds of the urethra and the vascular striations are well marked and are more pronounced in the lower semicircle Under air distension the walls spring apart and transverse muscular rings become apparent under the mucosa. As air-pressure is increased these

disappear from view leaving a perfectly smooth glistening mucosal surface of yellowish pink tint from the emptying of the sub-mucosal vessels On cessation of air pressure the walls promptly collapse together Lacunæ of Morgagni are recognised in small numbers as small V-shaped pouches with a broad end directed towards the meatus. Littré s glands are numerous but are often invisible in health under full air inflation however some of their openings may be recognised as tiny apertures in the roof sides or floor of the bulbous urethra

The orifice of the membranous urethra and the openings of Cowper s ducts can be inspected in the fully distended urethra. The former appears as a horizontal crescentic hooded slit. The ducts of Cowper's glands open on the floor of the bulbous urethra and appear as two pear shaped orifices lying one on either side of the mid-line. Occasionally one orifice lies in front of the other or both ducts open into a V-shaped pouch The course of the ducts may be shown by a ridge in the mucosa proximal to their openings As the urethroscope is withdrawn the longitudinal folds gradually become less marked and the central figure becomes a vertical slit

In the *penile urethra* the central figure is small and circular the mucous surface is of lustrous rose-pink colour and the longitudinal folds of the mucous membrane and the vascular striations form a regular stellate pattern radiating from the central figure Elasticity of the urethra is marked slight air distension shows sub-mucosal circular muscular rings which disappear under increased pressure On the roof of the penile urethra the lacunæ of Morgagni are seen in varying numbers in the mid-line On either side lies a chain of Littré s glands. These glands are also irregularly scattered on the lateral walls and on the floor of the urethra occurring in greatest frequency in the region of the peno-scrotal junction and immediately

proximal to the fossa navicularis. In the region of the *fossa navicularis* the central figure is in the form of a small vertical ovoid slit the mucous membrane is of pale yellow colour and shows no longitudinal folds or vascular striation This area is highly inelastic and un responsive to attempted air dilatation The lacuna magna (valve of Guérin) is visible on the roof about one inch proximal to the external urinary meatus.

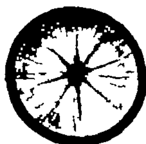


Fig 53
Urethroscopic appearances of normal penile urethra

Urethroscopic Appearances in the Diseased Anterior Urethra.—The morbid changes occurring in the urethra during the sub-acute or chronic stages of gonorrhoea depend to a great extent upon the acuteness and duration of the initial infection and the degree of success attending any treatment applied. The urethroscopic picture seen is often complex but can be resolved into several factors

(1) Alterations in the colour lustre and appearance of the urethral mucous membrane
(2) Alteration in the elasticity of the urethra.
(3) Pathological changes affecting the lacunæ of Morgagni and the glands of Littré

In acute gonorrhoea the initial inflammatory reaction produced is increased vascularity and small round cell

infiltration of the affected tissues leading to uniform angry redness congestion and oedema of the mucous membrane and obliteration of the normal longitudinal folds. As the disease continues a progressive connective tissue proliferation occurs tending to the deposition of fibrous tissue and causing alteration in the elasticity of the urethra These processes continue to a greater or less degree throughout the course of a gonococcal infection complete or partial spontaneous resolution may however occur at any time

Infiltrations.—According to the degree of fibrosis which has occurred infiltrations may be classified as soft transitional or hard In soft infiltration with minimal fibrous tissue deposition the mucous membrane is red and velvety in appearance often with localised darker red erosions of the epithelium or granulating areas. The central figure is regular the radiating folds are smaller in number wider and bleed easily At this stage the elasticity of the urethra is unaltered There is usually concomitant involvement of the Littré s glands

Further deposition and organisation of fibrous tissue in the affected areas leads to an alteration in the character and appearance of the infiltration Gradually the urethral mucous membrane becomes less congested the central figure becomes more irregular and often stellate the radiating folds are asymmetrical and deeply marked Under air pressure dilatation is sluggish and often unequal in different portions of the urethra when the air pressure is released collapse is delayed or the urethral canal may remain patent after the endoscope is partially withdrawn Fibrous streaks are not infrequently seen in the mucosa (stage of transitional infiltration)

Later the mucous membrane becomes blanched the columnar epithelium is replaced by the squamous type the surface is uneven irregular and frequently nacreous

often there is a patchy loss of epithelium. The urethra becomes highly inelastic from the sub-mucosal organisation of diffuse or localised masses of fibrous tissue (stage of hard infiltration)

Soft infiltrations of the urethra cause no difficulty in the introduction of an endoscopic tube transitional infiltrations may cause some gripping as the cannula is passed

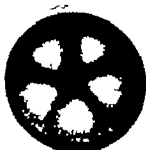


FIG 54
Soft infiltration under slight dilatation

hard infiltrations (stricture) prevent th passage of the instrument and permit the inspection only of the distal aspect of the lesion nearest the meatus

Morbid Appearances of Urethral Glandular Structures.—Involvement of the glands of Littré and the lacunæ of Morgagni is an invariable accompaniment of urethritis. Normally Littré's glands secrete a clear mucus infection is indicated by the alteration of the exudate to muco-pus or pus. The openings of the gland ducts normally inconspicuous show as angry red points often raised and papilliform and surrounded by a zone of hyperæmia. In some cases the affected gland-ducts are seen as open pockets in the mucosa, discharging muco-pus or in the later stages viscid mucoid material. Occlusion of the ducts may result in abscess formation or in the formation o

cysts. These latter may also occur in the more advanced stages of infiltration and appear as small yellowish rounded projections into the lumen of the urethra. Patchy or stellate deposits of fibrous tissue are often observed surrounding the orifices of the gland ducts and radiating into the surrounding mucous membrane The pathological

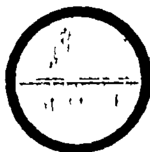


FIG 155.

(*Top*) Normal Littré glands seen under complete distension of urethra
(*Below*) Early sub mucous filtration and varying degrees of involvement of Littré's glands

changes observed in the lacunæ of Morgagni are closely similar

Resolution of soft or transitional infiltration and of the glandular involvement follows the institution of urethral dilatation at regular intervals There is gradual resorption of fibrous tissue the colour and appearance of the mucous membrane and its glandular openings gradually return to normal the elasticity of the urethra is restored While trans-urethroscopic treatment by medicated probe knife or electric cautery is seldom indicated it is of importance that the progress of the individual case should be observed by repeated endoscopy

Posterior Urethroscopy.—Visual examination of the posterior urethra is less frequently carried out than anterior urethroscopy. A greater degree of skill in manipulation of the instrument is required, and the utmost gentleness is necessary to avoid causing hæmorrhage which may render satisfactory examination impossible. The patient is examined in the lithotomy position, the operator sitting between the patient's knees. After the anterior and posterior urethræ have been anæsthetised the endoscopic tube with its obturator in position is lubricated and passed along the penile urethra until the tip reaches the junction of the bulbous and membranous urethræ. The beak should be directed towards the floor of the distal part of the urethra, and rotated towards the roof as the bulb is approached. Depression of the external end of the cannula, aided if necessary by a supporting finger on the perineum causes the tip of the instrument to enter the posterior urethra along which it is directed until the point reaches the level of the vesical sphincter. The obturator is withdrawn and the visual field is dried by swabbing and the optical and lighting devices attached.

The verumontanum is seen to project forwards into the window of the urethroscopic tube, the prostatic utricle being visible in the mid line with the minute openings of the common ejaculatory ducts on either side. Laterally the prostatic sinuses are seen as longitudinal fossæ on either side of the verumontanum. The orifices of the prostatic ducts are frequently not recognisable in health or have an appearance similar to that of the openings of Littré's glands. The mucous membrane has a much redder appearance than that of the anterior urethra and has not the same lustre or vascular striations. The central figure is that of an inverted U, the upward projection being due to the verumontanum around which the superior

cysts. These latter may also occur in the more advanced stages of infiltration and appear as small yellowish rounded projections into the lumen of the urethra. Patchy or stellate deposits of fibrous tissue are often observed surrounding the orifices of the gland ducts and radiating into the surrounding mucous membrane. The pathological

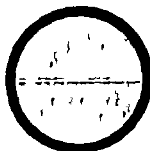


FIG. 135.
(*Top*) Normal Littré's gland seen under complete r distension of urethra
(*Below*) Early sub-mucous infiltration and varying degrees of volvement f Littré glands

changes observed in the lacunæ of Morgagni are closely similar.

Resolution of soft or transitional infiltrations and of the glandular involvement follows the institution of urethral dilatation at regular intervals. There is gradual resorption of fibrous tissue, the colour and appearance of the mucous membrane and its glandular openings gradually return to normal, the elasticity of the urethra is restored. While trans-urethroscopic treatment by medicated probe, knife or electric cautery is seldom indicated, it is of importance that the progress f the individual case should be observed by repeated endos py.

examined in the Trendelenberg position to prevent seepage of urine from obscuring the urethroscopic picture. The cannula with its obturator fitted is passed along the urethra until the tip enters the bladder The obturator is with drawn, and the bladder emptied by a soft rubber catheter passed through the endoscopic tube. The visual and lighting systems are now attached and the trigone of the bladder inspected. As the urethroscope is gradually withdrawn the vesical sphincter is observed to close behind it The mucous membrane of the urethra is smooth lustrous of a pale pink colour and is thrown into longitudinal folds. Glandular openings are infrequently seen. Imme diately proximal to the external meatus the orifices of Skene s tubules are seen on the floor or sides of the urethra.

The pathological conditions found in gonococcal infection of the female urethra are closely similar namely injection and oedema of the mucous membrane submucous infiltrations and infection of the glandular structures.

walls fall closely in folds more numerous and delicate than those of the anterior urethra Behind the verumontanum the prostatic fossette is seen extending to the neck of the bladder As the urethroscope is withdrawn the projection formed by the verumontanum disappears abruptly before the distal portion of the prostatic urethra is reached.

Inflammatory changes of the *prostatic urethra* cause a peculiar dull, velvety cyanotic colour of the mucosa, most marked over the verumontanum the prostatic utricle is gaping and discharges muco-pus or pus. The orifices of the common ejaculatory ducts, commonly slit like and of the same colour as the surrounding mucous membrane become more rounded are slightly raised above the contiguous surface and are encircled by a hyperaemic inflammatory zone As the condition progresses the orifices become dilated with everted pouting edges. The orifices of the prostatic ducts are seldom visible in health but in disease undergo changes very closely similar to those in the Littré's glands of the anterior urethra. In the later stages of infection sub-epithelial fibrosis occurs, causing irregular sclerotic plaques or granulating areas on the mucous membrane The verumontanum becomes shrunken and flattened and the orifices of the ejaculatory ducts stenosed.

The mucous membrane of the healthy *membranous urethra* is lustrous of a dark red hue striated with yellow and has numerous delicate longitudinal folds. Glandular structures are scanty When viewed by the urethroscope the central figure is punctiform and is surrounded by many fine radiating folds Air dilatation shows the canal to be highly elastic from the action of the compressor urethræ muscle The changes resulting from gonococcal infection correspond to those seen in the infiltrative process in the anterior urethra.

Urethroscopy in the Female.—The patient should be

lation postulation or ulceration or rarely a small elastic nodule 3 to 10 mm in diameter more deeply situated in the tissues, is found. In the male the common sites in order of frequency are the coronal sulcus the glans penis the inner aspect of the prepuce, and the urethra In the female the lesion may be apparent on the vulva. The sore usually heals spontaneously and rapidly

Adenitis.—Stiffness and aching in the groins especially on walking, may precede or call attention to the adenitis



FIG 56
Lymphogran loma nguinale showing adenitis of left groin nd multiple sinuses of right groi

which becomes apparent in from one to six weeks after the appearance of the genital sore Lymphangitis of painless character infrequently occurs At first the enlarged glands are discrete slightly tender firm and mobile. Later they become matted together (peri-adenitis) fluctuation occurs the skin assumes a purplish colour becomes adherent to the underlying mass and multiple sinuses form. In the absence of treatment the sinuses heal in from two to twelve months leaving thick puckered scars.

Constitutional symptoms may be slight or marked

CHAPTER XXI

OTHER CONDITIONS COMMONLY REFERRED TO VENEREAL DISEASE DEPARTMENTS

IN addition to those diseases already referred to in the differential diagnosis of the venereal diseases a number of conditions are not infrequently referred to the special departments because of the similarity of the symptoms and signs. In general these fall into one of three groups —

(1) *Genital ulcerations* e g lymphogranuloma inguinale ulcus acutum vulvæ or granuloma inguinale tropicum

(2) *Genital discharges* resulting from e g balanoposthitis non-gonococcal urethritis non-gonococcal vaginitis trichomonas vaginalis infestation vaginal thrush

(3) *Skin conditions* e g scabies impetigo genital warts, in which the genital lesions suggest syphilitic infection

LYMPHOGRANULOMA INGUINALE

(*Poradenitis*)

Lymphogranuloma inguinale is a virus infection characterised by subacute or chronic inflammatory changes in the inguinal and iliac groups of lymph glands frequently leading to suppuration and the formation of intractable sinuses in the groin The primary lesion occurs from three days to three weeks after exposure is usually single and consists of a painless herpetiform vesicle of circular or ovoid contour varying from 1 to 4 mm in diameter Less frequently a raised papule with slight central vesicu-

lation, pustulation or ulceration or rarely a small elastic nodule 3 to 10 mm in diameter more deeply situated in the tissues, is found In the male the common sites in order of frequency are the coronal sulcus the glans penis the inner aspect of the prepuce and the urethra. In the female the lesion may be apparent on the vulva. The sore usually heals spontaneously and rapidly

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Constitutional symptoms may be slight or mar

Lassitude prostration anorexia vomiting loss of weight and fever of irregular or intermittent type occur Articular pains may be complained of without apparent local changes or may be associated with diffuse swelling about the joints. Erythema nodosum may appear six or eight weeks after the commencement of glandular enlargement.

Complications —Complications in the male occur in the late stages of the disease and include elephantiasis of the penis scrotum and lower limbs Stricture of the rectum may occur in males but is more frequent in females In the female elephantiasis vulvæ and rectal stricture are not uncommon Infection of the male urethra with the lymphogranuloma inguinale virus gives rise to an intractable urethritis characterised by a mucoid or mucopurulent discharge Urethral stricture and sinus formation may be sequelæ Certain cases of urethritis without other clinical evidence of lymphogranuloma inguinale infection characterised by chronicity and a sago-grain appearance of the urethral mucosa (' sago-grain or Waelch urethritis) give positive reactions with Frei s antigen suggesting infection with the lymphogranuloma inguinale virus or some closely allied organism

Diagnosis —Lymphogranuloma inguinale must be differentiated from the manifestations of syphilis chancroid ulcerating granuloma of the pudenda and other genital ulcerations while the adenitis must be distinguished from that following tuberculous infection The clinical course transience of the genital lesions followed by slowly progressive intractable adenitis with later multiple sinus formation presents a clear-cut clinical picture which should not be confused with other possibilities. The possibility of syphilis must be excluded by dark-ground examination of the initial sore and by subsequent Wassermann observation it must be remembered that transient false positive serological reactions can occur in lympho-

granuloma inguinale Chancroid is excluded by a negative Reenstierna test Frei s test (an intradermal reaction with emulsion of the specific virus prepared from the pus from bubos of known cases or from the brain of mice infected by intracerebral inoculation) is specific. A positive reaction is noted in twenty four to forty-eight hours as a palpable dome-shaped inflammatory papule surrounded by an area of erythema Vesiculation, pustulation or central ulceration may occur The Frei test may remain positive for life in cases of lymphogranuloma inguinale or may become negative several years after the infection is healed.

Treatment —Rest in bed adequate simple diet and tonics are essential. Anaemia if present should be adequately treated Antisyphilitic treatment is ineffective Many cases react promptly to sulphapyridine sulphathiazole or sulphadiazine or to antimony compounds—antimony and potassium tartrate or stibenyl Pyrexial therapy if available, is the treatment of choice A series of fevers induced by physical measures or by the intravenous injection of Pyrifer *B coli* or T A.B vaccine is followed by rapid healing of the lesions Surgical intervention should be avoided in the early stages extensive surgical excision of the affected glands is followed by elephantiasis of the lower limbs In long-standing cases fistulæ may require to be opened up and plugged with B I P P iodoform gauze, or sulphonamide powder applied

ULCUS ACUTUM VULVÆ

Ulcus acutum vulvæ is a rapidly progressive acutely painful ulceration of the vulva due to *B crassus* The disease commonly occurs between the ages of fourteen and twenty but is not infrequently met with later in life. The areas involved in order of frequency are the inner aspects of the labia minora and majora the interlabial

fold the vaginal introitus and the fossa navicularis. The lesions may be solitary but are commonly multiple. Shallow or deep round ovoid or irregular ulcers appear with a soft greyish white or *yellowish* base A bright red inflammatory areola is often present Acute local burning pains are complained of and there is not infrequently inflammatory œdema of the labia Some degree of fever may accompany the ulceration which is progressive and may extend through the integument to involve the deeper tissues. Regional adenitis is absent

In the absence of treatment the disease may run a self limiting course healing tending to occur in about two weeks. Relapse is however common and spontaneous cure may be followed by almost immediate recurrence.

Diagnosis —Ulcus acutum vulvæ has to be differentiated from other acute painful genital ulcerations notably *chancroid. The more acute course the tendency to rapid* spontaneous cure ability to demonstrate *B crassus* in the *lesion and a negative Reenstierna test complete the* differentiation

Treatment —In view of the liability to spontaneous cure and recurrence it is difficult to assess the value of treatment Cleansing of the local lesions and painting with 1 per cent. gentian violet or dusting with sulphonamide powder are of value in relieving the symptoms and promoting cure Orally sodium salicylate (grs xxx t d.s) may be followed by dramatic results. Alternatively the ulphonamides, or vitamin C may cur rapidly

GRANULOMA INGUINALE TROPICUM

(Ulcerating Granuloma of the Pudenda)

Granuloma inguinale tropicum is a contagious ulcerative process invariably a sociated with Donovan bodies which are found within the mononuclear cells and characterised

by extensive tissue destruction and scar formation. The disease is more common in negroes and especially women. The initial lesion commences as a papule which enlarges and forms an ulcer with an irregular undermined edge and a base of dirty-grey granulomatous tissue there is a profuse malodorous discharge The ulcer spreads peripherally the advancing border being raised nodular and glazed. Secondary lesions occur from auto-inoculation. Hypertrophic vegetations spring from the base of the ulcers giving rise to papillomatous fungating masses. Healing is by dense bands of scar tissue which lead to local disfigurement or to mechanical elephantiasis from pressure on the lymph vessels. Multiple sinuses may persist in the scar tissue for long periods. Despite the chronicity of granuloma inguinale tropicum the regional lymph glands are not enlarged.

The diagnosis depends ultimately on the exclusion by the appropriate tests of other causes of genital ulceration, and on the demonstration of Donovan bodies in the mononuclear cells of the lesion. The condition generally reacts to intravenous injections of antimony and potassium tartrate. The commencing dose is 1 to 3 c.c. of 1 per cent. solution the dose being increased by 1 c.c on alternate days to a maximum of 10 to 12 c.c Other antimony preparations, *e g* stibophen may be employed. If this fails X rays or radium are indicated

BALANO-POSTHITIS

Inflammation of the mucous membrane covering the glans penis is called balanitis inflammation affecting the inner mucous aspect of the prepuce is termed posthitis. As inflammation usually affects both surfaces simultaneously the term balano-posthitis should be used. The condition is frequently associated with a phimosis which

may be congenital or acquired as a result of local inflammatory œdema.

Symptoms and Signs—There is usually some degree of heat and itching or irritation referred to the glans and to the prepuce. Dysuria and frequency of micturition may be complained of On examination a sickly smelling whitish yellow discharge is found to be exuding from the preputial meatus Retraction of the prepuce reveals a brightly reddened mucous membrane with its folds thickened from submucosal œdema. The superficial epithelium is macerated and shed exposing the papillæ, and leading to superficial erosions or later deeper ulcerations Irregular islands of whitish epithelium are frequently left The inguinal lymph glands may be slightly enlarged and tender inflammatory œdema or lymphangitis may render the prepuce irretractible phagedenic gangrene may rarely supervene



Fig 57
Balano-posthitis show g super ficial erosions and narrow bright red areola.

Diagnosis—An appreciation of the various causes of sub-preputial discharge and complete examination of the individual case will lead to the establishment of the true diagnosis and avoid many common errors. A sub-preputial discharge associated with dysuria may be confused with gonorrhœa or the institution of treatment on a hasty diagnosis of balanitis may ignore the possibility of a sub-preputial primary sore The possible causes of balano-posthitis or of sub-preputial discharge may be summarised —

(1) *Inflammatory*

(*a*) *Specific infections* —

Secondary to gonococcal urethritis.

Sub-preputial chancre or lesions of secondary or tertiary syphilis.

Sub-preputial chancroid.

Trichomonatous infestation of the sub-preputial sac.

Fuso-spirillary (Vincent) infections

(b) *Non-specific infections* —

Non-specific infection of the sub-preputial sac following sexual exposure or secondary to any cause of non-specific urethritis

(c) *Traumatic* —

Following the use of unsuitable or over strong antiseptics as prophylactics less commonly idiosyncrasy to the chemicals or contraceptives employed.

(2) *Constitutional*

Smegma accumulation the result of personal neglect may lead to the formation of concretions with later mechanical ulceration and secondary infection. Glycosuria chronic irritation of the sub-preputial sac from local deposit of urinary sugar in diabetes is a not infrequent cause of balano-posthitis.

(3) *Neoplastic*

Sub-preputial papillomata

Sub-preputial epitheliomata.

Careful local examination should enable the clinician to reach a diagnosis or indicate the necessary investigations

Treatment —Until the cause of a balano-posthitis has been discovered, and the possibility of syphilis provisionally excluded no local applications should be made which might prejudice the demonstration of *T pallidum* If the prepuce is retractible the maintenance of local cleanliness—

by thorough washing with saline followed by drying of the glans and preputial sac and heavy dusting with powdered sulphur or the application of Dermevan* (a vitaminised streptocide cream containing 25 per cent w/v sulphonamide) will *promote the healing of many cases of* simple or non-specific balano-posthitis After exclusion of syphilis stronger antiseptic applications may be of value—1 per cent. picric acid in spirit 10 per cent. resorcin in glycerine or a dusting powder of ½ to 1 per cent ac. salicyl in talc. In other cases the treatment of the underlying cause primary sore chancroid gonorrhœa diabetes etc. on the accepted principles is carried out concomitantly and results in cure.

Inflammatory phimosis with inability to retract the prepuce should be treated by copious sub-preputial irrigation with normal or hypertonic saline at a temperature of 110 to 115 F four hourly and the intermediate application of hot fomentations of 50 per cent magnesium sulphate solution Dorsal slitting of the prepuce or complete circumcision may be required if there is doubt as to the nature of the underlying lesion if the condition does not improve under conservative treatment or if phagedena supervenes

NON-GONOCOCCAL URETHRITIS AND VAGINITIS

Apart from gonorrhœa numerous acute inflammatory infections of the male urethra or of the urethra and vagina of the female may occur the symptoms and signs of which often closely simulate a true gonorrhœa. The various causes of urethral and vaginal discharge have already been considered in the differential diagnosis of gonorrhœa and it is only necessary here to emphasise the importance of the complete clinical and bacteriological

investigation of any suspected case to determine the ætiology and direct the course of treatment.

TRICHOMONATOUS INFESTATION

Trichomonatous infestation is not uncommon in the female but is less frequently recognised in the male. In the former the presence of trichomonas vaginalis in the vagina is associated with a definite train of symptoms. Itching and burning of the external genitalia occur; occasionally a dull aching pain referred to the lower abdominal quadrants is complained of. There is a profuse, frequently malodorous vaginal discharge.

Clinical examination reveals a greater or lesser degree of vulvitis with frequently an intertrigo extending down the inner aspect of the thighs. On separating the labia an abundant greenish yellow or greyish thin frothy discharge of low pH is noted. The vaginal mucous membrane appears thin and shows marked inflammatory and desquamative changes; desquamation over the vaginal rugæ in the milder cases gives rise to characteristic strawberry patches or in more severe cases to a generalised "raw beef" appearance. The changes involve the whole extent of the vagina and the vaginal portion of the cervix uteri, stopping short at the squamo-mucosal junction of the external os. The urethra is not infrequently involved and the organisms may reach the bladder or even the kidneys giving rise to symptoms of cystitis or pyelitis.

The importance of the recognition of the trichomonatous infestation lies in its not infrequent association with gonococcal infection. Demonstration of the gonococcus may be difficult or even impossible until the profuse discharge has abated under treatment. Persistence of a trichomonatous vaginitis is also a common cause of protraction of gonococcal infection.

Diagnosis—Confirmation of the clinical diagnosis of trichomonatous vaginitis depends on the recognition of the causal protozoon This may conveniently be done by the dark ground examination of fresh moist preparations, by the microscopic examination of films stained by Leishmann's method or by cultures. Dark-ground examination of fresh secretion is easily available and satisfactory The parasite has a body length of 16μ to 28μ and is recognised by its jerky movements of partial rotation and by the observation of the rapid movements of the four anterior flagella or of the undulating membrane

Treatment—Complete cure of trichomonatous infestation is possible only by protracted treatment Local cleansing by moist swabbing with green soap solution is followed by complete painting of the vagina and vaginal portion of the cervix with 1 per cent solution of gentian violet or 1 per cent lactic acid and the insertion into the posterior and lateral fornices of three acetarsone pessaries —(S V C (M and B) or Devegan (Bayer)) This treatment should be repeated daily and gradually diminished in frequency according to the clinical improvement After the condition has apparently cleared the patient should be advised to return for a single treatment immediately after the menstrual period during the next three to four months to prevent relapse which most frequently occurs at this time Silver picrate treatment has been advocated as an alternative for cases failing to respond After preliminary cleansing 5 gm of silver picrate-kaolin powder ("picragol") is insufflated into the vagina. This is followed by the nightly insertion for six nights of one silver picrate-boroglycerine pessary This sequence should be repeated for two to three weeks

In males trichomonatous infestation may involve (1) the subpreputial sac (2) the anterior urethra and (3)

the posterior urethra with possible extension to the prostate and seminal vesicles. Involvement of the subpreputial sac may give rise to slight local irritation or burning and a subpreputial discharge. On retraction of the prepuce a generalised balano-posthitis of varying severity is found. In the absence of concomitant involvement of the urethra these cases are readily cured by local cleanliness. Infestation of the anterior urethra may cause no symptoms or a varying degree of local irritation and dysuria A urethral discharge is almost invariably present varying in type from a scanty mucoid secretion to a very profuse purulent discharge. Extension to the posterior urethra gives rise to a chronic relapsing prostato-vesiculitis, the symptoms being those of a mild pyogenic infection Epididymitis may occur

Diagnosis—The diagnosis of trichomonatous infestation in the male depends on the demonstration of trichomonas vaginalis in smears or cultures. The possibility of this infestation must be remembered in cases of non specific infections more especially if the consort is found to be suffering from a trichomonous vaginitis.

Treatment—A strongly alkaline urine relieves the dysuria and frequency of micturition and inhibits the further development of the trichomonads. A permanent cure may follow large dosage of potassium citrate (grs. xl q d.s.) for fourteen to twenty-one days. Urethral instillations of an acetarsone emulsion are of value. Relapse is frequent and may be precipitated by alcohol or local irritative treatment

VAGINAL THRUSH

Infection of the vagina with oidium albicans is common in pregnancy or in association with glycosuria and gives rise to vaginal discharge and irritation. The discharge may be light or profuse and frequently consists of caseous

or inspissated secretion irritation is the predominant symptom frequently has a nocturnal periodicity and may be so severe as to prevent sleep On examination yellowish white patches may be found on the moist aspects of the vulva or on the surface of the vagina and cervix These patches are slightly adherent to the under lying surface and when removed leave a raw non bleeding area.

Diagnosis—The possibility of vaginal thrush is suggested by the predominant complaint of irritation by the clinical appearances and by the ability to demonstrate oïdium albicans in smears made from the whitish patches. The vaginal secretion is frequently mucoid and of a high pH Gram-stained smears show the presence of pus and epithelial cells the presence of Döderlein's bacillus in large numbers long hyphal filaments of the fungus and oval blastospores. Possible gonococcal infection should be excluded by routine smears and cultures. The thrush patches may be confused with the mucous patches of secondary syphilis *T pallidum* is however absent and the serological reactions are negative

Treatment—Local cleansing followed by painting of the affected areas with 1 per cent gentian violet solution procures immediate relief Painting should be carried out for three successive days the frequency being later reduced according to the clinical and symptomatic results Recurrence is not infrequent especially in cases occurring during pregnancy In these cases it may be necessary to continue treatment to term the disease undergoing spontaneous cure after delivery In cases failing to react to gentian violet weak alcoholic solution of iodine or *Lugol's* iodine may be used

GENITAL WARTS

(*Condylomata Acuminata Verruca Acuminata*)

Genital warts may occur in the male or female and may be associated with gonorrhœa trichomonatous infestation or other causes of local irritation or discharge. They are however of the same nature and due to the same virus as warts occurring elsewhere modification in appearance and rate of growth being due to the moist situation. In the



FIG 58
Penile warts in male

male warts commonly occur on the glans penis coronal sulcus, inner aspect of the prepuce and infrequently intra-urethrally In the female they are usually limited to the vulva but may spread to the vaginal walls or the cervix.

Diagnosis —Genital warts must be distinguished from the condylomata lata of secondary syphilis by the clinical appearances by the failure to demonstrate *T pallidum* and by the negative serology or if they form extensive plaques from pemphigus vegetans by the absence of umbilical and oral bullæ

or less frequently plum colour in and immediately proximal to the coronal sulcus Pressure on the deeper veins may result in œdema of the glans penis. In the absence of treatment ulceration occurs affecting the dorsal aspect of the constriction ring and may progress sufficiently to afford spontaneous relief This ulceration must carefully be differentiated from other forms of genital ulceration

Treatment —If the condition is recent and the œdema is slight reduction can usually be effected by grasping the shaft of the penis between the fore and ring fingers of *both hands placed immediately proximal to the constriction* ring and pressing steadily with the thumbs on the glans penis. If œdema is marked reduction may be accomplished after application of a 50 per cent. magnesium sulphate fomentation to the œdematous area and tight application of a rubber bandage Multiple punctures with a hypodermic needle aid in getting rid of the tissue œdema. If these measures fail the dorsal aspect of constricting band should be incised under local anæsthesia. Circumcision can be completed at a later date. Any associated lesions found should receive the appropriate treatment

INDEX

A

B

F

G

H

L

M

Y